

Sequence Summary of HuCAL-Fab1 Library

VL

Framework 1										CDR 1										Framework 2										CDR 2																																								
1										2										3										4										5																														
Position	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9																					
	EcoRV										BstXI										PstI										KpnI										SseXI										AseI										SmaDI									
VLx1	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	G	I	S	-	-	-	S	Y	L	A	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	A	A	S	S	L	Q	S	G	V	P								
VLx2	D	I	V	M	T	Q	S	P	L	S	L	P	V	T	P	G	E	P	A	S	I	S	C	R	S	S	Q	S	L	L	H	S	-	N	G	Y	N	Y	L	D	W	Y	L	Q	K	P	G	Q	S	P	Q	L	L	I	Y	L	G	S	N	R	A	S	G	V	P					
VLx3	D	I	V	L	T	Q	S	P	A	T	L	S	L	S	P	G	E	R	A	T	L	S	C	R	A	S	Q	S	V	S	-	-	-	S	Y	L	A	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I	Y	G	A	S	S	R	A	T	G	V	P								
VLx4	D	I	V	M	T	Q	S	P	D	S	L	A	V	S	L	G	E	R	A	T	I	N	C	R	S	S	Q	S	V	L	Y	S	S	N	K	N	Y	L	A	W	Y	Q	Q	K	P	G	Q	P	P	K	L	L	I	Y	W	A	S	T	R	E	S	G	V	P						
VL11	D	I	V	L	T	Q	P	P	-	S	V	S	G	A	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I	G	S	-	-	-	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	Y	D	N	Q	R	P	S	G	V	P							
VL12	D	I	A	L	T	Q	P	A	-	S	V	S	G	S	P	G	Q	S	I	T	I	S	C	T	G	T	S	S	D	V	G	G	Y	-	-	N	Y	V	S	W	Y	Q	Q	H	P	G	K	A	P	K	L	M	I	Y	D	V	S	N	R	P	S	G	V	S						
VL13	D	I	E	L	T	Q	P	P	-	S	V	S	V	A	P	G	Q	T	A	R	I	S	C	S	G	D	A	L	G	D	-	-	-	K	Y	A	S	W	Y	Q	Q	K	P	G	Q	A	P	V	L	V	I	Y	D	D	S	D	R	P	S	G	I	P								
EnvOv	BstXI										SseXI										KpnI										XmaI										BstXI										Bsu36I																			

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Fig. 1a

VH

Framework 1																				CDR 1										Framework 2										CDR 2																									
1										2										3										4										5										6															
M1el																				BspEI																				BspXI										XhoI															
Position	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0															
VH1A	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	S	S	V	K	V	S	C	K	A	S	G	G	T	F	S	S	-	-	Y	A	I	S	W	V	R	Q	A	P	G	Q	G	L	E	W	M	G	I	L	P	-	-	I	F	G	T	A	N	Y	A	
VH1B	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	S	S	V	K	V	S	C	K	A	S	G	G	T	F	T	S	-	-	Y	Y	M	H	W	V	R	Q	A	P	G	Q	G	L	E	W	M	G	I	N	P	-	-	N	S	G	G	T	N	Y	A	
VH2	Q	V	Q	L	K	E	S	G	P	A	L	V	K	P	T	Q	T	L	T	L	T	C	T	F	S	G	F	S	L	S	T	S	G	V	G	V	W	I	R	Q	A	P	G	K	A	L	E	W	L	A	L	I	O	-	-	-	W	D	D	K	Y	Y	S		
VH3	Q	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	-	-	Y	A	M	S	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	A	I	S	G	-	-	S	G	G	S	T	Y	Y	A	
VH4	Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	G	S	G	G	S	T	S	-	-	Y	Y	W	S	W	I	R	Q	P	P	G	K	G	L	E	W	I	G	I	Y	-	-	Y	S	G	S	T	N	Y	N			
VH5	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	S	E	S	L	K	I	S	C	K	G	S	G	Y	S	F	T	S	-	-	Y	W	I	G	W	V	R	Q	M	P	G	K	L	E	W	M	G	I	I	V	P	-	-	G	D	S	D	T	R	Y	S
VH6	Q	V	Q	L	Q	S	G	P	G	L	V	K	P	S	Q	T	L	S	L	T	C	A	I	S	G	D	S	V	S	S	N	S	A	A	W	W	I	R	Q	S	P	G	R	G	L	E	W	L	G	R	T	Y	Y	R	-	-	S	K	W	Y	N	D	Y	A	

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[illegible]

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7A

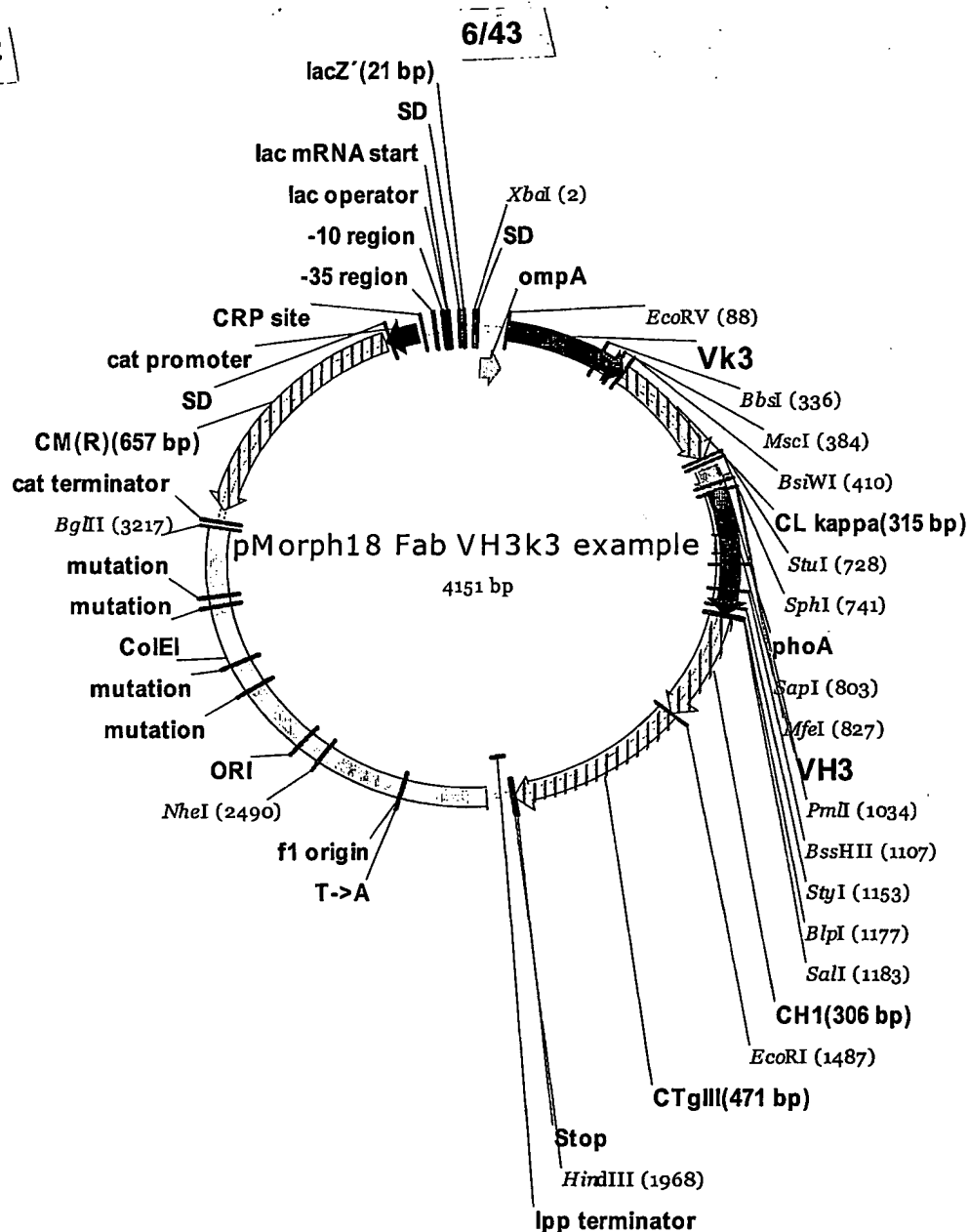
VH

Position		Framework 1																				CDR 1										Fr										
		1										2										3																				
		MseI																				BspEI										BspXI										
1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	a	b	2	3	4	5	6	7	8	9	0	1										
CAG	GTG	CAA	TTG	GTG	CAG	TCT	GGC	GGG	GAA	GTG	AAA	AAA	CGG	GGC	AGC	AGC	GTG	AAA	GTG	AGC	TGC	AAA	GCC	TCC	GGA	GGC	ACT	TTT	AGC	AGC	-	-	TAT	GCG	ATT	AGC	TGG	GTG	CQC	CAA	GCC	CCT
CAG	GTG	CAA	TTG	GTG	CAG	AGC	GGC	CGG	GAA	GTG	AAA	AAA	CGG	GGC	CGG	AGC	GTG	AAA	GTG	AGC	TGC	AAA	GCC	TCC	GGA	TAT	ACC	TTT	ACC	AGC	-	-	TAT	TAT	ATG	CAC	TGG	GTG	CQC	CAA	GCC	CCT
CAG	GTG	CAA	TTG	AAA	GAA	AGC	GGC	CGG	GCC	CTG	GTG	AAA	CGG	ACC	CAA	ACC	CTG	ACC	CTG	ACC	TGT	ACC	TTT	TCC	GGA	TTT	AGC	CTG	TCC	AGC	TCT	GGC	GTG	GAT	GGC	ATT	CQC	CAG	CGG	CCT		
CAG	GTG	CAA	TTG	GTG	GAA	AGC	GGC	GGC	CTG	GTG	AAA	CGG	GGC	GGC	CTG	GST	CTG	AGC	CTG	AGC	TGC	GCC	TCC	TCC	GGA	TTT	ACC	TTT	AGC	AGC	-	-	TAT	GCG	ATG	AGC	TGG	GTG	CQC	CAA	GCC	CCT
CAG	GTG	CAA	TTG	CAA	GAA	AGT	GGT	CGG	GGC	CTG	GTG	AAA	CGG	AGC	GAA	ACC	CTG	AGC	CTG	AGC	TGC	ACC	GTT	TCC	GGA	GGC	AGC	ATT	AGC	AGC	-	-	TAT	TAT	TGG	AGC	TGG	ATT	CQC	CAG	CGG	CCT
CAG	GTG	CAA	TTG	GTG	CAG	AGC	GGC	CGG	GAA	GTG	AAA	AAA	CGG	GGC	GAA	AGC	CTG	AAA	ATT	AGC	TGC	AAA	GGT	TCC	GGA	TAT	TCC	TTT	AGC	AGC	-	-	TAT	TGG	ATT	GGC	TGG	GTG	CQC	CAG	ATG	CCT
CAG	GTG	CAA	TTG	CAA	CAG	TCT	GGT	CGG	GGC	CTG	GTG	AAA	CGG	AGC	CMA	ACC	CTG	AGC	CTG	ACC	TGT	CGG	ATT	TCC	GGA	GAT	AGC	GTG	AGC	AAC	AGC	AGC	GCG	TGG	AGC	TGG	ATT	CQC	CAG	TCT	CCT	

Framework 2

	COR 3	Framework 4
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Fig. 2



	lacZ'	SD	ompA	
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	XbaI			

			M K K T A I A I A V	
1	TCTAGATAAC	GAGGGCAAAA	AATGAAAAAG	ACAGCTATCG CGATTGCAGT
	AGATCTATTG	CTCCCGTTTT	TTACTTTTTC	TGTCGATAGC GCTAACGTCA
				Vk3

		ompA		

			EcoRV	

	A L A G F A T V A Q	A D I V L T Q		
51	GGCACTGGCT	GGTTTCGCTA	CCGTAGCGCA	GGCCGATATC GTGCTGACCC

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Fig. 2 cont.

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CCGTGACCGA CCAAAGCGAT GGCATCGCGT CCGGCTATAG CACGACTGGG
Vk3
-----
  S P A T L S L S P G E R A T L S
101 AGAGCCCGGC GACCCTGAGC CTGTCTCCGG GCGAACGTGC GACCCTGAGC
TCTCGGGCCG CTGGGACTCG GACAGAGGCC CGCTTGACAG CTGGGACTCG
Vk3
-----
  C R A S Q S V S S S Y L A W Y Q Q
151 TGCAGAGCGA GCCAGAGCGT GAGCAGCAGC TATCTGGCGT GGTACCAGCA
ACGTCTCGCT CGGTCTCGCA CTCGTCTGTCG ATAGACCGCA CCATGGTCGT
Vk3
-----
  K P G Q A P R L L I Y G A S S R A
201 GAAACCAGGT CAAGCACCGC GTCTATTAAT TTATGGCGCG AGCAGCCGTG
CTTTGGTCCA GTTCGTGGCG CAGATAATTA AATACCGCGC TCGTCGGCAC
Vk3
-----
  T G V P A R F S G S G S G T D F
251 CAACTGGGGT CCCGGCGCGT TTTAGCGGCT CTGGATCCGG CACGGATTTT
GTTGACCCCA GGGCCGCGCA AAATCGCCGA GACCTAGGCC GTGCCTAAAA
Vk3
-----
                                BbsI
                                -----
  T L T I S S L E P E D F A V Y Y C
301 ACCCTGACCA TTAGCAGCCT GGAACCTGAA GACTTTGCGG TGTATTATTG
TGGGACTGGT AATCGTCGGA CCTTGGACTT CTGAAACGCC ACATAATAAC
Vk3
-----
                                MscI
                                -----
  Q Q H Y T T P P T F G Q G T K V E
351 CCAGCAGCAT TATACCACCC CGCCGACCTT TGGCCAGGGT ACGAAAGTTG
GGTCGTCGTA ATATGGTGGG GCGGCTGGAA ACCGGTCCCA TGCTTTCAAC
CL kappa
-----
Vk3
-----
                                BsiWI
                                -----
  I K R T V A A P S V F I F P P S
401 AAATTAAACG TACGGTGGCT GCTCCGAGCG TGTTTATTTT TCCGCCGAGC
TTTAATTTGC ATGCCACCGA CGAGGCTCGC ACAAATAAAA AGGCGGCTCG
CL kappa
-----
  D E Q L K S G T A S V V C L L N N
451 GATGAACAAC TGAAAAGCGG CACGGCGAGC GTGGTGTGCC TGCTGAACAA
CTACTTGTTG ACTTTTCGCC GTGCCGCTCG CACCACACGG ACGACTTGTT
CL kappa
-----
  F Y P R E A K V Q W K V D N A L Q
501 CTTTATATCCG CGTGAAGCGA AAGTTCAGTG GAAAGTAGAC AACGCGCTGC
GAAAATAGGC GCACTTCGCT TTCAAGTCAC CTTTCATCTG TTGCGCGACG
CL kappa
-----
  S G N S Q E S V T E Q D S K D S
551 AAAGCGGCAA CAGCCAGGAA AGCGTGACCG AACAGGATAG CAAAGATAGC
TTTCGCCGTT GTCGGTCCTT TCGCACTGGC TTGTCCTATC GTTTCATATC
CL kappa
-----

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Fig. 2 cont.

```

      T Y S L S S T L T L S K A D Y E K .
601  ACCTATTCTC TGAGCAGCAC CCTGACCCTG AGCAAAGCGG ATTATGAAAA
      TGGATAAGAG ACTCGTCGTG GGACTGGGAC TCGTTTCGCC TAATACTTTT
      CL kappa
      ~~~~~
      . H K V Y A C E V T H Q G L S S P V .
651  ACATAAAGTG TATGCGTGCG AAGTGACCCA TCAAGGTCTG AGCAGCCCCG
      TGTATTTTAC ATACGCACGC TTCACTGGGT AGTTCCAGAC TCGTCGGGCC
      CL kappa
      ~~~~~
                                StuI      SphI
                                ~~~~~
      . T K S F N R G E A
701  TGACTAAATC TTTTAATCGT GGCGAGGCCT GATAAGCATG CGTAGGAGAA
      ACTGATTTAG AAAATTAGCA CCGCTCCGGA CTATTCGTAC GCATCCTCTT
      phoA
      ~~~~~
                                SapI
                                ~~~~~
      M K Q S T I A L A L L P L L F .
751  AATAAAATGA AACAAAGCAC TATTGCACTG GCACTCTTAC CGTTGCTCTT
      TTATTTTACT TTGTTTCGTG ATAACGTGAC CGTGAGAATG GCAACGAGAA
      VH3
      ~~~~~
      phoA
      ~~~~~
      SapI                                MfeI
      ~~~~~
      . T P V T K A Q V Q L V E S G G G L .
801  CACCCCTGTT ACCAAAGCCG AAGTGCAATT GGTGGAAAGC GGCGGCGGCC
      GTGGGGACAA TGGTTTCGGC TTCACGTAA CCACCTTTCG CCGCCGCCGG
      VH3
      ~~~~~
      . V Q P G G S L R L S C A A S G F
851  TGGTGCAACC GGGCGGCAGC CTGCGTCTGA GCTGCGCGGC CTCCGGATTT
      ACCACGTTGG CCCGCCGTCG GACGCAGACT CGACGCGCCG GAGGCCTAAA
      VH3
      ~~~~~
      T F S S Y A M S W V R Q A P G K G .
901  ACCTTTAGCA GCTATGCGAT GAGCTGGGTG CGCCAAGCCC CTGGGAAGGG
      TGGAAATCGT CGATACGCTA CTCGACCCAC GCGGTTTCGG GACCCTTCCC
      VH3
      ~~~~~
      . L E W V S A I S G S G G S T Y Y A .
951  TCTCGAGTGG GTGAGCGCGA TTAGCGGTAG CGGCGGCAGC ACCTATTATG
      AGAGCTCACC CACTCGCGCT AATCGCCATC GCCGCCGTCG TGGATAATAC
      VH3
      ~~~~~
                                PmlI
                                ~~~~~
      . D S V K G R F T I S R D N S K N
1001 CGGATAGCGT GAAAGGCCGT TTTACCATT CACGTGATAA TTCGAAAAAC
      GCCTATCGCA CTTTCCGGCA AAATGGTAAA GTGCACTATT AAGCTTTTTG
      VH3
      ~~~~~
      T L Y L Q M N S L R A E D T A V Y .
1051 ACCCTGTATC TGCAATGAA CAGCCTGCGT GCGGAAGATA CGGCCGTGTA
      TGGGACATAG ACGTTTACTT GTCGGACGCA CGCCTTCTAT GCCGGCACAT
      VH3
      ~~~~~
      BssHII

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800S 2

9/43/94 Fig. 2 cont.

1101 . Y C A R W G G D G F Y A M D Y W G .
 TTATTGCGCG CGTTGGGGCG GCGATGGCTT TTATGCGATG GATTATTGGG
 AATAACGCGC GCAACCCCGC CGCTACCGAA AATACGCTAC CTAATAACCC
 CH1

VH3

SallI

StyI

BlnI

1151 . Q G T L V T V S S A S T K G P S
 GCCAAGGCAC CCTGGTGACG GTTAGCTCAG CGTCGACCAA AGGTCCAAGC
 CGGTTCCGTG GGACCACTGC CAATCGAGTC GCAGCTGGTT TCCAGGTTTC
 CH1

1201 V F P L A P S S K S T S G G T A A .
 GTGTTTCCGC TGGCTCCGAG CAGCAAAGC ACCAGCGGCG GCACGGCTGC
 CACAAAGGCG ACCGAGGCTC GTCGTTTTTCG TGGTCGCCGC CGTGCCGACG
 CH1

1251 . L G C L V K D Y F P E P V T V S W .
 CCTGGGCTGC CTGGTTAAAG ATTATTTCCC GGAACCAAGTC ACCGTGAGCT
 GGACCCGACG GACCAATTTT TAATAAAGGG CCTTGGTCAG TGGCACTCGA
 CH1

1301 . N S G A L T S G V H T F P A V L
 GGAACAGCGG GGCGCTGACC AGCGGCGTGC ATACCTTTCC GGCGGTGCTG
 CCTTGTCGCC CCGCGACTGG TCGCCGCACG TATGGAAAGG CCGCCACGAC
 CH1

1351 Q S S G L Y S L S S V V T V P S S .
 CAAAGCAGCG GCCTGTATAG CCTGAGCAGC GTTGTGACCG TGCCGAGCAG
 GTTTCGTGCG CGGACATATC GGACTCGTCG CAACACTGGC ACGGCTCGTC
 CH1

1401 . S L G T Q T Y I C N V N H K P S N .
 CAGCTTAGGC ACTCAGACCT ATATTTGCAA CGTGAACCAT AAACCGAGCA
 GTCGAATCCG TGAGTCTGGA TATAAACGTT GCACTTGGTA TTTGGCTCGT
 CH1 CTgIII

EcoRI

1451 . T K V D K K V E P K S E F G G G
 ACACCAAAGT GGATAAAAAA GTGGAACCGA AAAGCGAATT CGGGGGAGGG
 TGTGGTTTCA CCTATTTTTT CACCTTGGCT TTTCGCTTAA GCCCCCTCCC
 CTgIII

1501 S G S G D F D Y E K M A N A N K G .
 AGCGGGAGCG GTGATTTTGA TTATGAAAAG ATGGCAAACG CTAATAAGGG
 TCGCCCTCGC CACTAAAACCT AATACTTTTC TACCGTTTGC GATTATTCCC
 CTgIII

1551 . A M T E N A D E N A L Q S D A K G .
 GGCTATGACC GAAAATGCCG ATGAAAACGC GCTACAGTCT GACGCTAAAG
 CCGATACTGG CTTTTACGGC TACTTTTGCG CGATGTCAGA CTGCGATTTC
 CTgIII

1601 . K L D S V A T D Y G A A I D G F
 GCAAACCTGA TTCTGTCGCT ACTGATTACG GTGCTGCTAT CGATGGTTTC

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Fig. 2 cont.

```

CGTTTGAAGT AAGACAGCGA TGAATAATGC CACGACGATA GCTACCAAAG
CTgIII
-----
  I G D V S G L A N G N G A T G D F .
1651 ATTGGTGACG TTTCCGGCCT TGCTAATGGT AATGGTGCTA CTGGTGATTT
TAACCACTGC AAAGGCCGGA ACGATTACCA TTACCACGAT GACCACTAAA
CTgIII
-----
  A G S N S Q M A Q V G D G D N S P .
1701 TGCTGGCTCT AATTCCCAAA TGGCTCAAGT CGGTGACGGT GATAATTCAC
ACGACCGAGA TTAAGGGTTT ACCGAGTTCA GCCACTGCCA CTATTAAGTG
CTgIII
-----
  L M N N F R Q Y L P S L P Q S V
1751 CTTTAATGAA TAATTTCCTT CAATATTTAC CTTCCCTCCC TCAATCGGTT
GAAATTACTT ATTAAAGGCA GTTATAAATG GAAGGGAGGG AGTTAGCCAA
CTgIII
-----
  E C R P F V F G A G K P Y E F S I .
1801 GAATGTGCGC CTTTGTCTT TGGCGCTGGT AAACCATATG AATTTTCTAT
CTTACAGCGG GAAAACAGAA ACCGCGACCA TTTGGTATAC TTAAAAGATA
CTgIII
-----
  D C D K I N L F R G V F A F L L Y .
1851 TGATTGTGAC AAAATAAACT TATTCCTGGT TGTCTTTGCG TTTCTTTTAT
ACTAACACTG TTTTATTTGA ATAAGGCACC ACAGAAACGC AAAGAAAATA
CTgIII
-----
  V A T F M Y V F S T F A N I L R
1901 ATGTTGCCAC CTTTATGTAT GTATTTTCTA CGTTTGCTAA CATACTGCGT
TACAACGGTG GAAATACATA CATAAAAGAT GCAAACGATT GTATGACGCA
CTgIII
-----
                                Stop                lpp terminator
                                ---
                                HindIII
                                ~~~~~

  N K E S
1951 AATAAGGAGT CTTGATAAGC TTGACCTGTG AAGTGAAAAA TGGCGCAGAT
TTATTCCTCA GAACTATTCG AACTGGACAC TTCACTTTTT ACCGCGTCTA
lpp terminator
-----
2001 TGTGCGACAT TTTTFTTGTG TGCCGTTTAA TGAAATTGTA AACGTTAATA
ACACGCTGTA AAAAAACAG ACGGCAAATT ACTTTAACAT TTGCAATTAT
-----
                                f1 origin
2051 TTTTGTGTTAA ATTGCGGTTA AATTTTGTG AAATCAGCTC ATTTTAAAC
AAAACAATTT TAAGCGCAAT TTAAAAACAA TTTAGTCGAG TAAAAAATTG
-----
                                f1 origin
2101 CAATAGGCCG AAATCGGCAA AATCCCTTAT AAATCAAAAG AATAGACCGA
GTTATCCGGC TTTAGCCGTT TTAGGGAATA TTTAGTTTTT TTATCTGGCT
-----
                                f1 origin
2151 GATAGGGTTG AGTGTGTGTC CAGTTTGGAA CAAGAGTCCA CTATTAAAGA
CTATCCCAAC TCACAACAAG GTCAAACCTT GTTCTCAGGT GATAATTTCT
-----
                                f1 origin
2201 ACGTGGACTC CAACGTCAAA GGGCGAAAAA CCGTCTATCA GGGCGATGGC
TGCACCTGAG GTTGCAGTTT CCCGCTTTTT GGCAGATAGT CCCGCTACCG
-----

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f1 origin

Fig. 2 cont.

T->A

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2251  CCACTACGAG AACCATCACC CTAATCAAGT TTTTGGGGT CGAGGTGCCG
      GGTGATGCTC TTGGTAGTGG GATTAGTTCA AAAAACCCCA GCTCCACGGC
      ~~~~~
              f1 origin
2301  TAAAGCACTA AATCGGAACC CTAAAGGGAG CCCCCGATTT AGAGCTTGAC
      ATTTTCGTGAT TTAGCCTTGG GATTTCCCTC GGGGGCTAAA TCTCGAACTG
      ~~~~~
              f1 origin
2351  GGGGAAAGCC GCGAACGTG GCGAGAAAGG AAGGGAAGAA AGCGAAAGGA
      CCCCTTTTCGG CCGCTTGACAC CGCTCTTTCC TTCCCTTCTT TCGCTTTTCT
      ~~~~~
              f1 origin
2401  GCGGGCGCTA GGGCGCTGGC AAGTGTAGCG GTCACGCTGC GCGTAACCAC
      CGCCCCGGAT CCCGCGACCG TTCACATCGC CAGTGCACG CGCATTGGTG
      ~~~~~
              f1 origin
              ~~~~~
              NheI
2451  CACACCCGCC GCGCTTAATG CGCCGCTACA GGGCGCGTGC TAGCCATGTG
      GTGTGGGCGG CGCGAATTAC GCGGCGATGT CCCGCGCACG ATCGGTACAC
      ~~~~~
              f1 origin
              ~~~~~
              ColeI
2501  AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG
      TCGTTTTCCG GTCGTTTTCC GGTCTTGGC ATTTTTCCGG CGCAACGACC
      ~~~~~
              ColeI
              ~~~~~
              ORI
              ~~~~~
2551  CGTTTTTCCA TAGGCTCCGC CCCCCTGACG AGCATCACAA AAATCGACGC
      GCAAAAAGGT ATCCGAGGCG GGGGGACTGC TCGTAGTGTT TTAGCTGCG
      ~~~~~
              ColeI
2601  TCAAGTCAGA GGTGGCGAAA CCGACAGGA CTATAAAGAT ACCAGGCGTT
      AGTTCAGTCT CCACCGCTTT GGGCTGTCCT GATATTTCTA TGGTCCGCAA
      ~~~~~
              ColeI
2651  TCCCCCTGGA AGCTCCCTCG TGCCTCTCTC TGTTCCGACC CTGCCGCTTA
      AGGGGGACCT TCGAGGGAGC ACGCGAGAGG ACAAGGCTGG GACGGCGAAT
      ~~~~~
              ColeI
              ~~~~~
              mutation
              ~~~~~
2701  CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAAGCGTGGC GCTTCTCAT
      GGCCTATGGA CAGGCGGAAA GAGGGAAGCC CTTGCGACCG CGAAAGAGTA
      ~~~~~
              ColeI
              ~~~~~
              mutation
              ~~~~~
2751  AGCTCACGCT GTAGGTATCT CAGTTCGGTG TAGGTCGTTT GCTCCAAGCT
      TCGAGTGCGA CATCCATAGA GTCAAGCCAC ATCCAGCAAG CGAGGTTCTGA
      ~~~~~
              ColeI
              ~~~~~
              mutation
              ~~~~~
2801  GGGCTGTGTG CACGAACCCC CCGTTCAGTC CGACCGCTGC GCCTTATCCG
      CCCGACACAC GTGCTTGGGG GGCAAGTCAG GCTGGCGACG CGGAATAGGC
      ~~~~~
              ColeI

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Fig. 2 cont.

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2851  GTAAC TATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG
      CATTGATAGC AGAACTCAGG TTGGGCCATT CTGTGCTGAA TAGCGGTGAC
      -----
                        ColEI
2901  GCAGCAGCCA CTGGTAACAG GATTAGCAGA GCGAGGTATG TAGGCGGTGC
      CGTCGTCGGT GACCATTGTC CTAATCGTCT CGCTCCATAC ATCCGCCACG
      -----
                        ColEI
                                                mutation
2951  TACAGAGTTC TTGAAGTGGT GGCCTAACTA CGGCTACACT AGAAGAACAG
      ATGTCTCAAG AACTTCACCA CCGGATTGAT GCCGATGTGA TCTTCTTGTC
      -----
                        ColEI
                        mutation
3001  TATTTGGTAT CTGCGCTCTG CTGTAGCCAG TTACCTTCGG AAAAAGAGTT
      ATAAACCATA GACGCGAGAC GACATCGGTC AATGGAAGCC TTTTCTCTAA
      -----
                        ColEI
3051  GGTAGCTCTT GATCCGGCAA ACAAAACCACC GCTGGTAGCG GTGGTTTTTT
      CCATCGAGAA CTAGGCCGTT TGTTTGGTGG CGACCATCGC CACCAAAAAA
      -----
                        ColEI
3101  TGTTTGCAAG CAGCAGATTA CGCGCAGAAA AAAAGGATCT CAAGAAGATC
      ACAACGTTTC GTCGTCTAAT GCGCGTCTTT TTTTCCTAGA GTTCTTCTAG
      -----
                        ColEI
3151  CTTTGATCTT TTCTACGGGG TCTGACGCTC AGTGGAACGA AACTCACGT
      GAAACTAGAA AAGATGCCCC AGACTGCGAG TCACCTTGCT TTTGAGTGCA
      -----
                        ColEI
                                                cat terminator
                        -----
                        BglII
                        -----
3201  TAAGGGATTT TGGTCAGATC TAGCACCAGG CGTTTAAGGG CACCAATAAC
      ATTCCCTAAA ACCAGTCTAG ATCGTGGTCC GCAAATTCCC GTGGTTATTG
      -----
                        ColEI
                        cat terminator
                        -----
3251  TGCCTTAAAA AAATTACGCC CCGCCCTGCC ACTCATCGCA GTACTGTTGT
      ACGGAATTTT TTTAATGCGG GCGGGGACGG TGAGTAGCGT CATGACAACA
      -----
                        CM (R)
3301  AATTCATTAA GCATTCTGCC GACATGGAAG CCATCACAAA CGGCATGATG
      TTAAGTAATT CGTAAGACGG CTGTACCTTC GGTAGTGTTT GCCGTACTAC
      -----
                        CM (R)
3351  AACCTGAATC GCCAGCGGCA TCAGCACCTT GTCGCCTTGC GTATAATATT
      TTGGACTTAG CGGTCGCCGT AGTCGTGGAA CAGCGGAACG CATATTATAA
      -----
                        CM (R)
3401  TGCCCATAGT GAAAACGGGG GCGAAGAAGT TGTCCATATT GGCTACGTTT
      ACGGGTATCA CTTTTGCCCC CGCTTCTTCA ACAGGTATAA CCGATGCAAA
      -----
                        CM (R)
3451  AAATCAAAAC TGGTGAAACT CACCCAGGGA TTGGCTGAGA CGAAAAACAT
      TTTAGTTTTG ACCACTTTGA GTGGGTCCCT AACCGACTCT GCTTTTTTGA
      -----

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Fig. 2 cont.

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                                CM (R)
3501  ATTCTCAATA AACCCCTTTAG GGAAATAGGC CAGGTTTTTCA CCGTAACACG
      TAAGAGTTAT TTGGGAAATC CCTTTATCCG GTCCAAAAGT GGCATTGTGC
      ~~~~~
                                CM (R)
3551  CCACATCTTG CGAATATATG TGTAGAAACT GCCGGAAATC GTCGTGGTAT
      GGTGTAGAAC GCTTATATAC ACATCTTTGA CGGCCTTTAG CAGCACCATA
      ~~~~~
                                CM (R)
3601  TCACTCCAGA GCGATGAAAA CGTTTCAGTT TGCTCATGGA AAACGGTGTA
      AGTGAGGTCT CGCTACTTTT GCAAAGTCAA ACGAGTACCT TTTGCCACAT
      ~~~~~
                                CM (R)
3651  ACAAGGGTGA ACACTATCCC ATATCACCAG CTCACCGTCT TTCATTGCCA
      TGTTCCTCACT TGTGATAGGG TATAGTGGTC GAGTGGCAGA AAGTAACGGT
      ~~~~~
                                CM (R)
3701  TACGGAACTC CGGGTGAGCA TTCATCAGGC GGGCAAGAAT GTGAATAAAG
      ATGCCTTGAG GCCCACTCGT AAGTAGTCCG CCCGTTCTTA CACTTATTTT
      ~~~~~
                                CM (R)
3751  GCCGGATAAA ACTTGTGCTT ATTTTCTTTT ACGGTCTTTA AAAAGGCCGT
      CGGCCTATTT TGAACACGAA TAAAAAGAAA TGCCAGAAAT TTTTCCGGCA
      ~~~~~
                                CM (R)
3801  AATATCCAGC TGAACGGTCT GGTATAGGT ACATTGAGCA ACTGACTGAA
      TTATAGGTCG ACTTGCCAGA CCAATATCCA TGTAACCTCGT TGACTGACTT
      ~~~~~
                                CM (R)
3851  ATGCCTCAAA ATGTTCTTTA CGATGCCATT GGGATATATC AACGGTGGTA
      TACGGAGTTT TACAAGAAAT GCTACGGTAA CCCTATATAG TTGCCACCAT
      ~~~~~
                                CM (R)
3901  TATCCAGTGA TTTTTTCTC CATTTTAGCT TCCTTAGCTC CTGAAAATCT
      ATAGGTCACT AAAAAAGAG GTAAAATCGA AGGAATCGAG GACTTTTAGA
      ~~~~~
                                CM (R)                                SD
                                ~~~~~
                                cat promoter
3951  CGATAACTCA AAAAATACGC CCGGTAGTGA TCTTATTTCA TTATGGTGAA
      GCTATTGAGT TTTTATGCG GGCCATCACT AGAATAAAGT AATACCACTT
      ~~~~~
                                cat promoter
                                CRP site
                                ~~~~~
4001  AGTTGGAACC TCACCCGACG TCTAATGTGA GTTAGCTCAC TCATTAGGCA
      TCAACCTTGG AGTGGGCTGC AGATTACACT CAATCGAGTG AGTAATCCGT
      ~~~~~
                                cat promoter
                                lac mRNA
start
                                ~
                                lac operator
                                ~~~~~
                                -35 region                                -10 region
                                ~~~~~                                ~~~~~
4051  CCCCAGGCTT TACACTTTAT GCTTCCGGCT CGTATGTTGT GTGGAATTGT
      GGGGTCCGAA ATGTGAAATA CGAAGGCCGA GCATACAACA CACCTTAACA
      lac operator                                SD                                lacZ'
      ~~~~~                                ~~~~~
4101  GAGCGGATAA CAATTCACA CAGGAAACAG CTATGACCAT GATTACGAAT

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Fig. 2 cont.

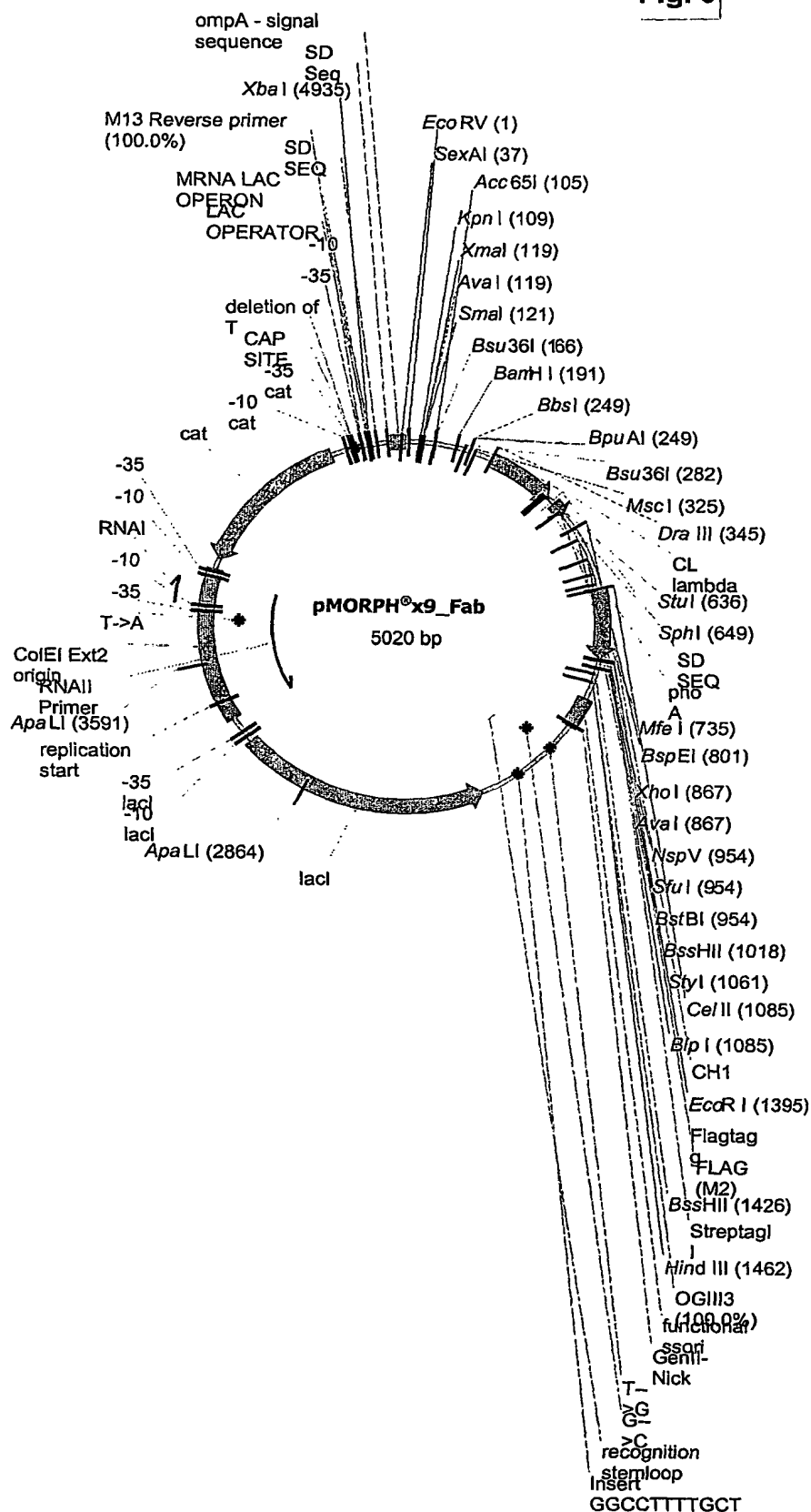
CTCGCCTATT GTTAAAGTGT GTCCTTTGTC GATACTGGTA CTAATGCTTA
lacZ⁻

4151

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T
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Fig. 3



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Fig. 3 cont.

EcoRV

SexAI

1 ATCGTGCTGA CCCAGCCGCC TTCAGTGAGT GGCGCACCAG GTCAGCGTGT
TAGCACGACT GGGTCGGCGG AAGTCACTCA CCGCGTGGTC CAGTCGCACA

51 GACCATCTCG TGTAGCGGCA GCAGCAGCAA CATTGGCAGC AACTATGTGA
CTGGTAGAGC ACATCGCCGT CGTCGTCTGT GTAACCGTCG TTGATACACT

XmaI

KpnI

SmaI

~~~~~

~~~~~

Acc65I

AvaI

~~~~~

~~~~~

101 GCTGGTACCA GCAGTTGCCG GGGACGGCGC CGAAACTGCT GATTTATGAT
CGACCATGGT CGTCAACGGG CCCTGCCGCG GCTTTGACGA CTAAATACTA

Bsu36I

BamHI

151 AACCAACCAGC GTCCCTCAGG CGTGCCGGAT CGTTTTAGCG GATCCAAAAG
TTGTTGGTCG CAGGGAGTCC GCACGGCCTA GCAAATCGC CTAGGTTTTC

BpuAI

~~~~~

BbsI

~~~~~

201 CGGCACCAGC GCGAGCCTTG CGATTACGGG CCTGCAAAGC GAAGACGAAG
GCCGTGGTCG CGCTCGGAAC GCTAATGCCC GGACGTTTCG CTTCTGCTTC

Bsu36I

~~~~~

251 CGGATTATTA TTGCCAGAGC TATGACATGC CTCAGGCTGT GTTTGGCGGC  
GCCTAATAAT AACGGTCTCG ATACTGTACG GAGTCCGACA CAAACCGCCG

MscI

DraIII

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~~~~~

301 GGCACGAAGT TTAACCGTTC TTGGCCAGCC GAAAGCCGCA CCGAGTGTGA  
CCGTGCTTCA AATTGGCAAG AACCGGTCGG CTTTCGGCGT GGCTCACACT

351 CGCTGTTTCC GCCGAGCAGC GAAGAATTGC AGGCGAACAA AGCGACCCTG  
GCGACAAAGG CGGCTCGTCG CTTCTTAACG TCCGCTTGTT TCGCTGGGAC

401 GTGTGCCTGA TTAGCGACTT TTATCCGGGA GCCGTGACAG TGGCCTGGAA  
CACACGGAAT AATCGCTGAA AATAGGCCCT CGGCACTGTC ACCGGACCTT

451 GGCAGATAGC AGCCCCGTCA AGGCGGGAGT GGAGACCACC ACACCCTCCA  
CCGTCTATCG TCGGGGCAGT TCCGCCCTCA CCTCTGGTGG TGTGGGAGGT

501 AACAAAGCAA CAACAAGTAC GCGGCCAGCA GCTATCTGAG CCTGACGCCT  
TTGTTTCGTT GTTGTTTCATG CGCCGGTCGT CGATAGACTC GGACTGCGGA

551 GAGCAGTGGA AGTCCCACAG AAGCTACAGC TGCCAGGTCA CGCATGAGGG  
CTCGTCACCT TCAGGGTGTC TTCGATGTCT ACGGTCCAGT GCGTACTCCC



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Fig. 3 cont.

StuI

SphI

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601 GAGCACCGTG GAAAAAACCG TTGCGCCGAC TGAGGCCTGA TAAGCATGCG  
CTCGTGGCAC CTTTTTTGGC AACGCGGCTG ACTCCGGACT ATTCGTACGC

651 TAGGAGAAAA TAAAATGAAA CAAAGCACTA TTGCACTGGC ACTCTTACCG  
ATCCTCTTTT ATTTTACTTT GTTTCGTGAT AACGTGACCG TGAGAATGGC

MfeI

~~~~~

701 TTGCTCTTCA CCCCTGTTAC CAAAGCCCAG GTGCAATTGA AAGAAAGCGG
AACGAGAAGT GGGGACAATG GTTTCGGGTC CACGTAACT TTCTTTCGCC

BspEI

~

751 CCCGGCCCTG GTGAAACCGA CCCAAACCCT GACCCTGACC TGTACCTTTT
GGGCCGGGAC CACTTTGGCT GGGTTTGGGA CTGGGACTGG ACATGGAAAA

BspEI

~~~~~

801 CCGGATTTAG CCTGTCCACG TCTGGCGTTG GCGTGGGCTG GATTCGCCAG  
GGCCTAAATC GGACAGGTGC AGACCGCAAC CGCACCCGAC CTAAGCGGTC

XhoI

~~~~~

AvaI

~~~~~

851 CCGCCTGGGA AAGCCCTCGA GTGGCTGGCT CTGATTGATT GGGATGATGA  
GGCGGACCCT TTCGGGAGCT CACCGACCGA GACTAACTAA CCCTACTACT

901 TAAGTATTAT AGCACCAGCC TGAAAACGCG TCTGACCATT AGCAAAGATA  
ATTCATAATA TCGTGGTCGG ACTTTTGCGC AGACTGGTAA TCGTTTCTAT

BstBI

~~~~~

SfuI

~~~~~

NspV

~~~~~

951 CTTCGAAAAA TCAGGTGGTG CTGACTATGA CCAACATGGA CCCGGTGGAT
GAAGCTTTTT AGTCCACCAC GACTGATACT GGTGTACCT GGGCCACCTA

BssHII

~~~~~

1001 ACGGCCACCT ATTATTGCGC GCGTTCTCCT CGTTATCGTG GTGCTTTTGA  
TGCCGGTGGA TAATAACGCG CGCAAGAGGA GCAATAGCAC CACGAAAACCT

BlnI

~~~~~

StyI

~~~~~

CeiII

~~~~~

1051 TTATTGGGGC CAAGGCACCC TGGTGACGGT TAGCTCAGCG TCGACCAAAG
AATAACCCCG GTTCCGTGGG ACCACTGCCA ATCGAGTCGC AGCTGGTTTC

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Fig. 3 cont.

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1101  GTCCAAGCGT  GTTTCCGCTG  GCTCCGAGCA  GCAAAAGCAC  CAGCGGCGGC
      CAGGTTTCGCA  CAAAGGCGAC  CGAGGCTCGT  CGTTTTTCGTG  GTCGCCGCCG

1151  ACGGCTGCCC  TGGGCTGCCT  GGTAAAGAT  TATTTCCCGG  AACCAGTCAC
      TGCCGACGGG  ACCCGACGGA  CCAATTTCTA  ATAAAGGGCC  TTGGTCAGTG

1201  CGTGAGCTGG  AACAGCGGGG  CGCTGACCAG  CGGCGTGCAT  ACCTTTCCGG
      GCACTCGACC  TTGTCGCCCC  GCGACTGGTC  GCCGCACGTA  TGGAAAGGCC

1251  CGGTGCTGCA  AAGCAGCGGC  CTGTATAGCC  TGAGCAGCGT  TGTGACCGTG
      GCCACGACGT  TTCGTCGCCG  GACATATCGG  ACTCGTCGCA  AACTGGCAC

1301  CCGAGCAGCA  GCTTAGGCAC  TCAGACCTAT  ATTTGCAACG  TGAACCATAA
      GGCTCGTCGT  CGAATCCGTG  AGTCTGGATA  TAAACGTTGC  ACTTGGTATT

                                     EcoRI
                                     ~~~~~~
1351  ACCGAGCAAC  ACCAAAGTGG  ATAAAAAAGT  GGAACCGAAA  AGCGAATTCG
      TGGCTCGTTG  TGGTTTCACC  TATTTTTTCA  CCTTGGCTTT  TCGCTTAAGC

                                     BssHII
                                     ~~~~~~
1401  ACTATAAAGA  TGACGATGAC  AAAGGCGCGC  CGTGGAGCCA  CCCGCAGTTT
      TGATATTTCT  ACTGCTACTG  TTTCCGCGCG  GCACCTCGGT  GGGCGTCAAA

                                     HindIII
                                     ~~~~~~
1451  GAAAAATGAT  AAGCTTGACC  TGTGAAGTGA  AAAATGGCGC  AGATTGTGCG
      CTTTTTACTA  TTCGAACTGG  AACTTCACT  TTTTACCGCG  TCTAACACGC

                                     OGIII3  100.0%
                                     =====

1501  ACATTTTTTT  TGTCTGCCGT  TTAATTAAAG  GGGGGGGGGG  GCCGGCCTGG
      TGTAAAAAAA  ACAGACGGCA  AATTAATTTT  CCCCCCCCCC  CGGCCGGACC

1551  GGGGGGGTGT  ACATGAAATT  GTAAACGTTA  ATATTTTGTG  AAAATTCGCG
      CCCCCCACCA  TGTACTTTAA  CATTTGCAAT  TATAAAACAA  TTTTAAGCGC

1601  TTAAATTTTT  GTTAAATCAG  CTCATTTTTT  AACCAATAGG  CCGAAATCGG
      AATTTAAAAA  CAATTTAGTC  GAGTAAAAAA  TTGGTTATCC  GGCTTTAGCC

1651  CAAAATCCCT  TATAAATCAA  AAGAATAGAC  CGAGATAGGG  TTGAGTGTTG
      GTTTTAGGGA  ATATTTAGTT  TTCTTATCTG  GCTCTATCCC  AACTCACAAC

1701  TTCCAGTTTG  GAACAAGAGT  CCACTATTAA  AGAACGTGGA  CTCCAACGTC
      AAGGTCAAAC  CTTGTTCTCA  GGTGATAATT  TCTTGACCT  GAGGTTGCAG

1751  AAAGGGCGAA  AAACCGTCTA  TCAGGGCGAT  GGCCCACTAC  GAGAACCATC
      TTTCCCGCTT  TTTGGCAGAT  AGTCCCGCTA  CCGGGTGATG  CTCTTGGTAG

1801  ACCCTAATCA  AGTTTTTTTG  GGTCGAGGTG  CCGTAAAGCA  CTAAATCGGA
      TGGGATTAGT  TCAAAAAACC  CCAGCTCCAC  GGCATTTCTG  GATTTAGCCT

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19/43 Fig. 3 cont.

1851 ACCCTAAAGG GAGCCCCCGA TTTAGAGCTT GACGGGGAAA GCCGGCGAAC
TGGGATTTCC CTCGGGGGCT AAATCTCGAA CTGCCCCCTT CGGCCGCTTG

1901 GTGGCGAGAA AGGAAGGGAA GAAAGCGAAA GGAGCGGGCG CTAGGGCGCT
CACCGCTCTT TCCTTCCCTT CTTTCGCTTT CCTCGCCCGC GATCCCGCGA

1951 GGCAAGTGTA GCGGTCACGC TCGCGTAAC CACCACACCC GCCGCGCTTA
CCGTTACAT CGCCAGTGCG ACGCGCATTG GTGGTGTGGG CGGCGCGAAT

2001 ATGCGCCGCT ACAGGGCGCG TGCTAGACTA GTGTTTAAAC CGGACCGGGG
TACGCGGCGA TGTCCCGCGC ACGATCTGAT CACAAATTTG GCCTGGCCCC

2051 GGGGGCTTAA GTGGGCTGCA AAACAAAACG GCCTCCTGTC AGGAAGCCGC
CCCCGAATT CACCCGACGT TTTGTTTTGC CGGAGGACAG TCCTTCGGCG

2101 TTTTATCGGG TAGCCTCACT GCCCGCTTTC CAGTCGGGAA ACCTGTCGTG
AAAATAGCCC ATCGGAGTGA CGGGCGAAAG GTCAGCCCTT TGGACAGCAC

2151 CCAGCTGCAT CAGTGAATCG GCCAACGCGC GGGGAGAGGC GGTTTGCGTA
GGTCGACGTA GTCACCTAGC CGGTTGCGCG CCCCTCTCCG CCAAACGCAT

2201 TTGGGAGCCA GGGTGGTTTT TCTTTTCACC AGTGAGACGG GCAACAGCTG
AACCCTCGGT CCCACCAAAA AGAAAAGTGG TCACTCTGCC CGTTGTCGAC

2251 ATTGCCCTTC ACCGCCTGGC CCTGAGAGAG TTGCAGCAAG CGGTCCACGC
TAACGGGAAG TGGCGGACCG GGACTCTCTC AACGTCGTTT GCCAGGTGCG

2301 TGGTTTGCCC CAGCAGGCGA AAATCCTGTT TGATGGTGGT CAGCGGCGGG
ACCAAACGGG GTCGTCCGCT TTTAGGACAA ACTACCACCA GTCGCCGCCC

2351 ATATAACATG AGCTGTCCTC GGTATCGTCG TATCCCACTA CCGAGATGTC
TATATTGTAC TCGACAGGAG CCATAGCAGC ATAGGGTGAT GGCTCTACAG

2401 CGCACCAACG CGCAGCCCGG ACTCGGTAAT GGCACGCATT GCGCCCAGCG
GCGTGGTTGC GCGTCGGGCC TGAGCCATTA CCGTGCGTAA CGCGGGTCGC

2451 CCATCTGATC GTTGGCAACC AGCATCGCAG TGGGAACGAT GCCCTCATTC
GGTAGACTAG CAACCGTTGG TCGTAGCGTC ACCCTTGCTA CGGGAGTAAG

2501 AGCATTTGCA TGGTTTGTG AAAACCGGAC ATGGCACTCC AGTCGCCTTC
TCGTAAACGT ACCAAACAAC TTTTGGCCTG TACCGTGAGG TCAGCGGAAG

2551 CCGTTCCGCT ATCGGCTGAA TTTGATTGCG AGTGAGATAT TTATGCCAGC
GGCAAGGCGA TAGCCGACTT AAATAACGC TCACTCTATA AATACGGTCG

2601 CAGCCAGACG CAGACGCGCC GAGACAGAAC TTAATGGGCC AGCTAACAGC
GTCGGTCTGC GTCTGCGCGG CTCTGTCTTG AATTACCCGG TCGATTGTGCG

2651 GCGATTTGCT GGTGGCCCAA TCGGACCAGA TGCTCCACGC CCAGTCGCGT
CGCTAAACGA CCACCGGGTT ACGCTGGTCT ACGAGGTGCG GGTCAGCGCA

2701 ACCGTCCTCA TGGGAGAAAA TAATACTGTT GATGGGTGTC TGGTCAGAGA
TGGCAGGAGT ACCCTCTTTT ATTATGACAA CTACCCACAG ACCAGTCTCT

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Fig. 3 cont.

2751 CATCAAGAAA TAACGCCGGA ACATTAGTGC AGGCAGCTTC CACAGCAATA
GTAGTTCTTT ATTGCGGCCT TGTAATCACG TCCGTCGAAG GTGTCGTTAT

2801 GCATCCTGGT CATCCAGCGG ATAGTTAATA ATCAGCCAC TGACACGTTG
CGTAGGACCA GTAGGTCGCC TATCAATTAT TAGTCGGGTG ACTGTGCAAC

ApaLI
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2851 CGCGAGAAGA TTGTGCACCG CCGCTTTACA GGCTTCGACG CCGCTTCGTT  
GCGCTCTTCT AACACGTGGC GGCGAAATGT CCGAAGCTGC GGCGAAGCAA

2901 CTACCATCGA CACGACCACG CTGGCACCCA GTTGATCGGC GCGAGATTTA  
GATGGTAGCT GTGCTGGTGC GACCGTGGGT CAACTAGCCG CGCTCTAAAT

2951 ATCGCCGCGA CAATTTGCGA CGGCGCGTGC AGGGCCAGAC TGGAGGTGGC  
TAGCGGCGCT GTTAAACGCT GCCGCGCACG TCCCGGTCTG ACCTCCACCG

3001 AACGCCAATC AGCAACGACT GTTTGCCCGC CAGTTGTTGT GCCACGCGGT  
TTGCGGTTAG TCGTTGCTGA CAAACGGGCG GTCAACAACA CGGTGCGCCA

3051 TAGGAATGTA ATTCAGCTCC GCCATCGCCG CTTCCACTTT TTTCCGCGTT  
ATCCTTACAT TAAGTCGAGG CGGTAGCGGC GAAGGTGAAA AAGGGCGCAA

3101 TTCGCAGAAA CGTGGCTGGC CTGGTTCACC ACGCGGGAAA CGGTCTGATA  
AAGCGTCTTT GCACCGACCG GACCAAGTGG TCGGCCCTTT GCCAGACTAT

3151 AGAGACACCG GCATACTCTG CGACATCGTA TAACGTTACT GGTTTCACAT  
TCTCTGTGGC CGTATGAGAC GCTGTAGCAT ATTGCAATGA CCAAAGTGTA

3201 TCACCACCCT GAATTGACTC TCTTCCGGGC GCTATCATGC CATAACGCGA  
AGTGGTGGGA CTTAACTGAG AGAAGGCCCG CGATAGTACG GTATGGCGCT

3251 AAGGTTTTGC GCCATTCGAT GCTAGCCATG TGAGCAAAAAG GCCAGCAAAA  
TTCCAAAACG CCGTAAGCTA CGATCGGTAC ACTCGTTTTT CGGTCGTTTT

3301 GGCCAGGAAC CGTAAAAAGG CCGCGTTGCT GGCGTTTTTC CATAGGCTCC  
CCGGTCCTTG GCATTTTTCC GGCGCAACGA CCGCAAAAAG GTATCCGAGG

3351 GCCCCCTGA CGAGCATCAC AAAAATCGAC GCTCAAGTCA GAGGTGGCGA  
CGGGGGGACT GTCGTAGTG TTTTtagctg CGAGTTCAGT CTCCACCGCT

3401 AACCCGACAG GACTATAAAG ATACCAGGCG TTTCCCCCTG GAAGCTCCCT  
TTGGGCTGTC CTGATATTTT TATGGTCCGC AAAGGGGGAC CTTGAGGGA

3451 CGTGCGCTCT CCTGTTCCGA CCCTGCCGCT TACCGGATAC CTGTCCGCCT  
GCACGCGAGA GGACAAGGCT GGGACGGCGA ATGGCCTATG GACAGGCGGA

3501 TTCTCCCTTC GGGAAGCGTG GCGCTTTCTC ATAGCTCACG CTGTAGGTAT  
AAGAGGGAAG CCCTTCGCAC CGCGAAAGAG TATCGAGTGC GACATCCATA

ApaLI  
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3551 CTCAGTTCGG TGTAGGTCGT TCGCTCCAAG CTGGGCTGTG TGCACGAACC
GAGTCAAGCC ACATCCAGCA AGCGAGGTTC GACCCGACAC ACGTGCTTGG

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Fig. 3 cont.

3601	CCCCGTTTCAG	CCCGACCGCT	GCGCCTTATC	CGGTAACTAT	CGTCTTGAGT
	GGGGCAAGTC	GGGCTGGCGA	CGCGGAATAG	GCCATTGATA	GCAGAACTCA
3651	CCAACCCGGT	AAGACACGAC	TTATCGCCAC	TGGCAGCAGC	CACTGGTAAC
	GGTTGGGCCA	TTCTGTGCTG	AATAGCGGTG	ACCGTCGTCG	GTGACCATTG
3701	AGGATTAGCA	GAGCGAGGTA	TGTAGGCGGT	GCTACAGAGT	TCTTGAAGTG
	TCCTAATCGT	CTCGCTCCAT	ACATCCGCCA	CGATGTCTCA	AGAACTTCAC
3751	GTGGCCTAAC	TACGGCTACA	CTAGAAGAAC	AGTATTTGGT	ATCTGCGCTC
	CACCGGATTG	ATGCCGATGT	GATCTTCTTG	TCATAAACCA	TAGACGCGAG
3801	TGCTGTAGCC	AGTTACCTTC	GGAAAAAGAG	TTGGTAGCTC	TTGATCCGGC
	ACGACATCGG	TCAATGGAAG	CCTTTTTCTC	AACCATCGAG	AACTAGGCCG
3851	AAACAAACCA	CCGCTGGTAG	CGGTGGTTTT	TTTGTTTGCA	AGCAGCAGAT
	TTTGTTTGGT	GGCGACCATC	GCCACCAAAA	AAACAAACGT	TCGTTCGTCTA
3901	TACGCGCAGA	AAAAAAGGAT	CTCAAGAAGA	TCCTTTGATC	TTTTCTACGG
	ATGCGCGTCT	TTTTTTCCTA	GAGTTCCTCT	AGGAAACTAG	AAAAGATGCC
3951	GGTCTGACGC	TCAGTGGAAC	GAAAACCTCAC	GTTAAGGGAT	TTTGGTCAGA
	CCAGACTGCG	AGTCACCTTG	CTTTTGAGTG	CAATTCCTTA	AAACCAGTCT
4001	TCTAGCACCA	GGCGTTTAAG	GGCACCAATA	ACTGCCTTAA	AAAAATTACG
	AGATCGTGGT	CCGCAAATTC	CCGTGGTTAT	TGACGGAATT	TTTTTAATGC
4051	CCCCGCCCTG	CCACTCATCG	CAGTACTGTT	GTAATTCATT	AAGCATTTCTG
	GGGGCGGGAC	GGTGAGTAGC	GTCATGACAA	CATTAAGTAA	TTCGTAAGAC
4101	CCGACATGGA	AGCCATCACA	AACGGCATGA	TGAACCTGAA	TCGCCAGCGG
	GGCTGTACCT	TCGGTAGTGT	TTGCCGTACT	ACTTGGACTT	AGCGGTCGCC
4151	CATCAGCACC	TTGTGCGCTT	GCGTATAATA	TTTGCCCATA	GTGAAAACGG
	GTAGTCGTGG	AACAGCGGAA	CGCATATTAT	AAACGGGTAT	CACTTTTGCC
4201	GGGCGAAGAA	GTTGTCCATA	TTGGCTACGT	TTAAATCAAA	ACTGGTGAAA
	CCCGCTTCTT	CAACAGGTAT	AACCGATGCA	AATTTAGTTT	TGACCACTTT
4251	CTCACCCAGG	GATTGGCTGA	GACGAAAAAC	ATATTCTCAA	TAAACCCTTT
	GAGTGGGTCC	CTAACCGACT	CTGCTTTTTG	TATAAGAGTT	ATTTGGGAAA
4301	AGGGAAATAG	GCCAGGTTTT	CACCGTAACA	CGCCACATCT	TGCGAATATA
	TCCCTTTATC	CGGTCCAAAA	GTGGCATTGT	GCGGTGTAGA	ACGCTTATAT
4351	TGTGTAGAAA	CTGCCGGAAG	TCGTCGTGGT	ATTCACCTCA	GAGCGATGAA
	ACACATCTTT	GACGGCCTTT	AGCAGCACCA	TAAGTGAGGT	CTCGCTACTT
4401	AACGTTTCAG	TTTGCTCATG	GAAAACGGTG	TAACAAGGGT	GAACACTATC
	TTGCAAAGTC	AAACGAGTAC	CTTTTGCCAC	ATTGTTCCCA	CTTGTGATAG
4451	CCATATCACC	AGCTCACCGT	CTTTCATTGC	CATACGGAAC	TCCGGGTGAG
	GGTATAGTGG	TCGAGTGGCA	GAAAGTAACG	GTATGCCTTG	AGGCCCACTC

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Fig. 3 cont.

4501 CATTTCATCAG GCGGGCAAGA ATGTGAATAA AGGCCGGATA AACTTTGTGC
GTAAGTAGTC CGCCCGTTCT TACTTATT TCCGGCCTAT TTTGAACACG

4551 TTATTTTTTCT TTACGGTCTT TAAAAAGGCC GTAATATCCA GCTGAACGGT
AATAAAAAGA AATGCCAGAA ATTTTCCCG CATTATAGGT CGACTTGCCA

4601 CTGGTTATAG GTACATTGAG CAACTGACTG AAATGCCTCA AAATGTTCTT
GACCAATATC CATGTAACCTC GTTGACTGAC TTTACGGAGT TTTACAAGAA

4651 TACGATGCCA TTGGGATATA TCAACGGTGG TATATCCAGT GATTTTTTTC
ATGCTACGGT AACCTATAT AGTTGCCACC ATATAGGTCA CTAAAAAAG

4701 TCCATTTTAG CTTCTTAGC TCCTGAAAAT CTCGATAACT CAAAAAATAC
AGGTAAAATC GAAGGAATCG AGGACTTTTA GAGCTATTGA GTTTTTTATG

4751 GCGCGGTAGT GATCTTATTT CATTATGGTG AAAGTTGGAA CCTCACCCGA
CGGGCCATCA CTAGAATAAA GTAATACCAC TTTCAACCTT GGAGTGGGCT

4801 CGTCTAATGT GAGTTAGCTC ACTCATTAGG CACCCCAGGC TTTACACTTT
GCAGATTACA CTCAATCGAG TGAGTAATCC GTGGGGTCCG AAATGTGAAA

4851 ATGCTTCCGG CTCGTATGTT GTGTGGAATT GTGAGCGGAT AACAATTTCA
TACGAAGGCC GAGCATACAA CACACCTTAA CACTCGCCTA TTGTTAAAGT

M13 Reverse primer 100.0% XbaI
===== ~~~~~

4901 CACAGGAAAC AGCTATGACC ATGATTACGA ATTTCTAGAT AACGAGGGCA
GTGTCCTTTG TCGATACTGG TACTAATGCT TAAAGATCTA TTGCTCCCGT

4951 AAAAATGAAA AAGACAGCTA TCGCGATTGC AGTGGCACTG GCTGGTTTCG
TTTTTACTTT TTCTGTCGAT AGCGCTAACG TCACCGTGAC CGACCAAAGC

EcoRV
~~~

5001 CTACCGTAGC GCAGGCCGAT  
GATGGCATCG CGTCCGGCTA

## 7A

MS-Roche #3  
MS-Roche #7  
MS-Roche #8

**MS-Roche #3**  
**MS-Roche #7**  
**MS-Roche #8**

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Fig. 4a cont.

| Framework 3 |   |   |   |   |   |   |   |   |   | CDR 3 |   |   |   |   |   |   |   |   |   | Framework 4 |   |   |   |   |   |   |   |   |   |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------|---|---|---|---|---|---|---|---|---|-------|---|---|---|---|---|---|---|---|---|-------------|---|---|---|---|---|---|---|---|---|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|             |   |   |   |   |   |   |   |   |   |       |   |   |   |   |   |   |   |   |   |             |   |   |   |   |   |   |   |   |   |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 6           |   |   |   |   |   |   |   |   |   | 9     |   |   |   |   |   |   |   |   |   | 10          |   |   |   |   |   |   |   |   |   |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| BamHI       |   |   |   |   |   |   |   |   |   | BstI  |   |   |   |   |   |   |   |   |   | MscI        |   |   |   |   |   |   |   |   |   | BstXI |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| V           | P | A | R | F | S | G | S | G | T | D     | F | T | L | T | I | S | S | L | E | P           | E | D | F | A | V | Y | C | Q | Q | V     | Y | N | P | P | - | V | T | F | G | Q | G | T | K | V | E | I | K | R | T |
| V           | P | A | R | F | S | G | S | G | T | D     | F | T | L | T | I | S | S | L | E | P           | E | D | F | A | T | Y | C | F | Q | L     | Y | S | D | P | - | F | T | F | G | Q | G | T | K | V | E | I | K | R | T |
| V           | P | A | R | F | S | G | S | G | T | D     | F | T | L | T | I | S | S | L | E | P           | E | D | F | A | T | Y | C | Q | Q | L     | S | S | F | P | - | P | T | F | G | Q | G | T | K | V | E | I | K | R | T |

|       |   |   |   |   |   |   |   |   |   |      |   |   |   |   |   |   |   |   |   |      |   |   |   |   |   |   |   |   |   |        |   |   |   |   |   |   |   |   |   |      |   |   |   |   |   |   |   |   |   |      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------|---|---|---|---|---|---|---|---|---|------|---|---|---|---|---|---|---|---|---|------|---|---|---|---|---|---|---|---|---|--------|---|---|---|---|---|---|---|---|---|------|---|---|---|---|---|---|---|---|---|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6     |   |   |   |   |   |   |   |   |   | 7    |   |   |   |   |   |   |   |   |   | 8    |   |   |   |   |   |   |   |   |   | 9      |   |   |   |   |   |   |   |   |   | 10   |   |   |   |   |   |   |   |   |   | 11   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 9     | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9    | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9    | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9      | 0 | 1 | 2 | 3 |   |   |   |   |   |      |   |   |   |   |   |   |   |   |   |      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| BstEI |   |   |   |   |   |   |   |   |   | NspV |   |   |   |   |   |   |   |   |   | EagI |   |   |   |   |   |   |   |   |   | BstHII |   |   |   |   |   |   |   |   |   | SylI |   |   |   |   |   |   |   |   |   | BspI |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Y     | A | D | S | V | K | G | G | R | F | T    | I | S | R | D | N | S | K | N | T | L    | Y | L | Q | M | N | S | L | R | A | E      | D | T | A | V | Y | Y | C | A | R | L    | T | H | Y | A | R | Y | Y | R | Y | F    | D | V | W | G | Q | G | T | L | V | T | V | S | S |   |   |   |   |
| Y     | A | D | S | V | K | G | G | R | F | T    | I | S | R | D | N | S | K | N | T | L    | Y | L | Q | M | N | S | L | R | A | E      | D | T | A | V | Y | Y | C | A | R | G    | K | G | N | T | H | K | P | Y | G | Y    | V | R | Y | F | D | V | W | G | Q | G | T | L | V | T | V | S | S |
| Y     | A | D | S | V | K | G | G | R | F | T    | I | S | R | D | N | S | K | N | T | L    | Y | L | Q | M | N | S | L | R | A | E      | D | T | A | V | Y | Y | C | A | R | L    | L | S | R | G | Y | N | G | Y | H | K    | F | D | V | W | G | Q | G | T | L | V | T | V | S | S |   |   |   |



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## 7A

# VH

| Framework 1 |     |     |     |     |     |     |     |     |     |     |     |     |     |     | CDR 1 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |   |     |     |     |     |     |     |     |     |     |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| 1           |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 2     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 3     |   |     |     |     |     |     |     |     |     |     |  |  |  |  | 4 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| MeI         |     |     |     |     |     |     |     |     |     |     |     |     |     |     | BspEI |     |     |     |     |     |     |     |     |     |     |     |     |     |     | BspXI |   |     |     |     |     |     |     |     |     |     |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1           | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 0   | 1   | 2   | 3   | 4   | 5   | 6     | 7   | 8   | 9   | 0   | 1   | a   | b   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9     | 0 |     |     |     |     |     |     |     |     |     |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| MS-Roche #3 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |   |     |     |     |     |     |     |     |     |     |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| CAG         | GTG | CAA | TTG | GTG | GAA | AGC | GGC | GGC | CTG | GTG | CAA | CCG | GGC | GGC | AGC   | CTG | CGT | CTG | AGC | TGC | GCG | GCC | TCC | GGA | TTT | ACC | TTT | AGC | AGC | -     | - | TAT | GCG | ATG | AGC | TGG | GTG | CQC | CAA | GCC |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| MS-Roche #7 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |   |     |     |     |     |     |     |     |     |     |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| CAG         | GTG | CAA | TTG | GTG | GAA | AGC | GGC | GGC | CTG | GTG | CAA | CCG | GGC | GGC | AGC   | CTG | CGT | CTG | AGC | TGC | GCG | GCC | TCC | GGA | TTT | ACC | TTT | AGC | AGC | -     | - | TAT | GCG | ATG | AGC | TGG | GTG | CQC | CAA | GCC |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| MS-Roche #8 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |       |   |     |     |     |     |     |     |     |     |     |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| CAG         | GTG | CAA | TTG | GTG | GAA | AGC | GGC | GGC | CTG | GTG | CAA | CCG | GGC | GGC | AGC   | CTG | CGT | CTG | AGC | TGC | GCG | GCC | TCC | GGA | TTT | ACC | TTT | AGC | AGC | -     | - | TAT | GCG | ATG | AGC | TGG | GTG | CQC | CAA | GCC |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

### Framework 3

### Framework 3

[illegible]

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Fig. 4b cont.

| Framework 4 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 10          |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| BstXI       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 3           | 4   | 5   | 6   | 7   | 8   | 9   | 0   | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| TTT         | GCG | GTT | TAT | TAT | TGC | CAG | CAG | GTT | TAT | AAT | CCT | CCT | GTT | ACC | TTT | GGC | CAG | GCG | ACG | AAA | GTT | GAA | ATT | AAA | CST | ACG |
| TTT         | GCG | ACT | TAT | TAT | TGC | TTT | CAG | CTT | TAT | TCT | GAT | CCT | TTT | ACC | TTT | GSC | CAG | GCG | ACG | AAA | GTT | GAA | ATT | AAA | CST | ACG |
| TTT         | GCG | ACT | TAT | TAT | TGC | CAG | CAG | CTT | TCT | TCT | TTT | CCT | CCT | ACC | TTT | GSC | CAG | GCG | ACG | AAA | GTT | GAA | ATT | AAA | CST | ACG |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
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|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
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|             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

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Fig. 5

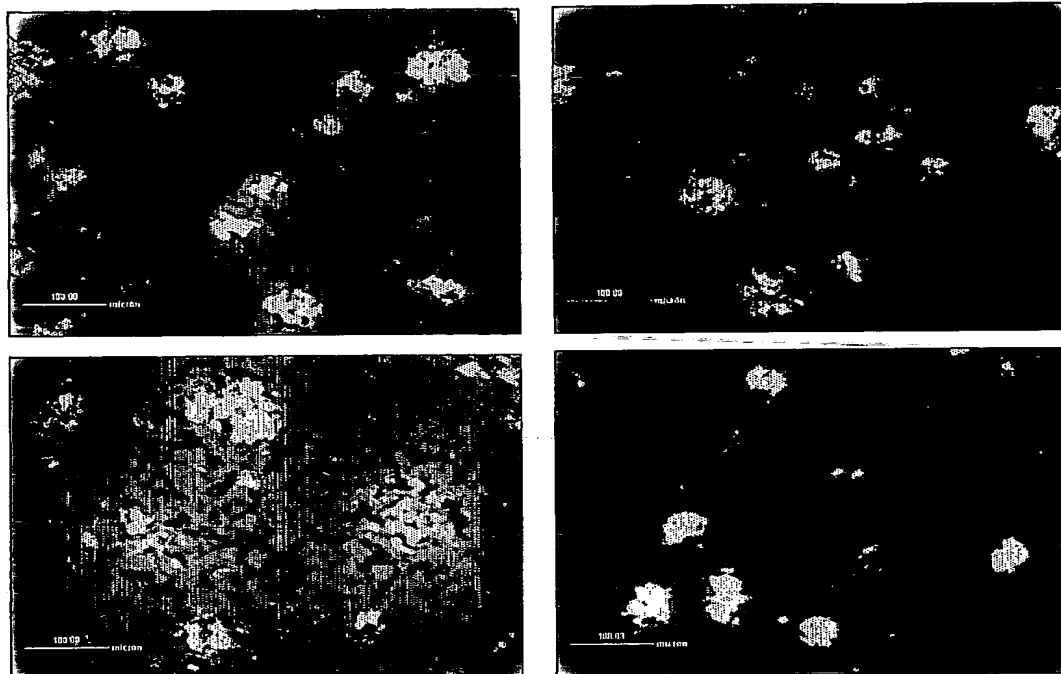
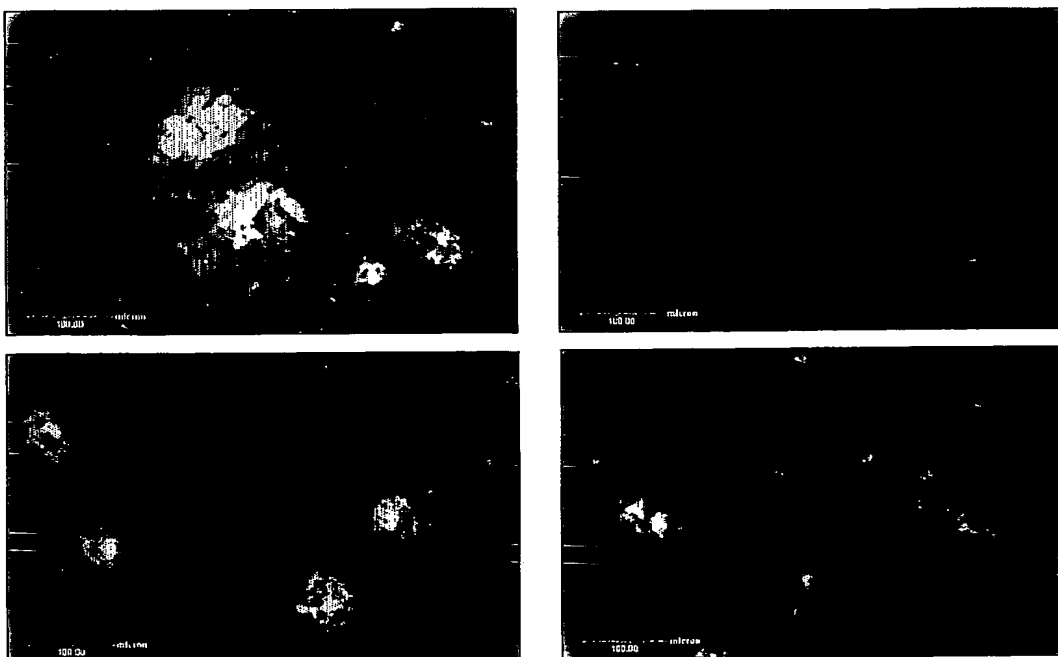


Fig. 6



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Fig. 7

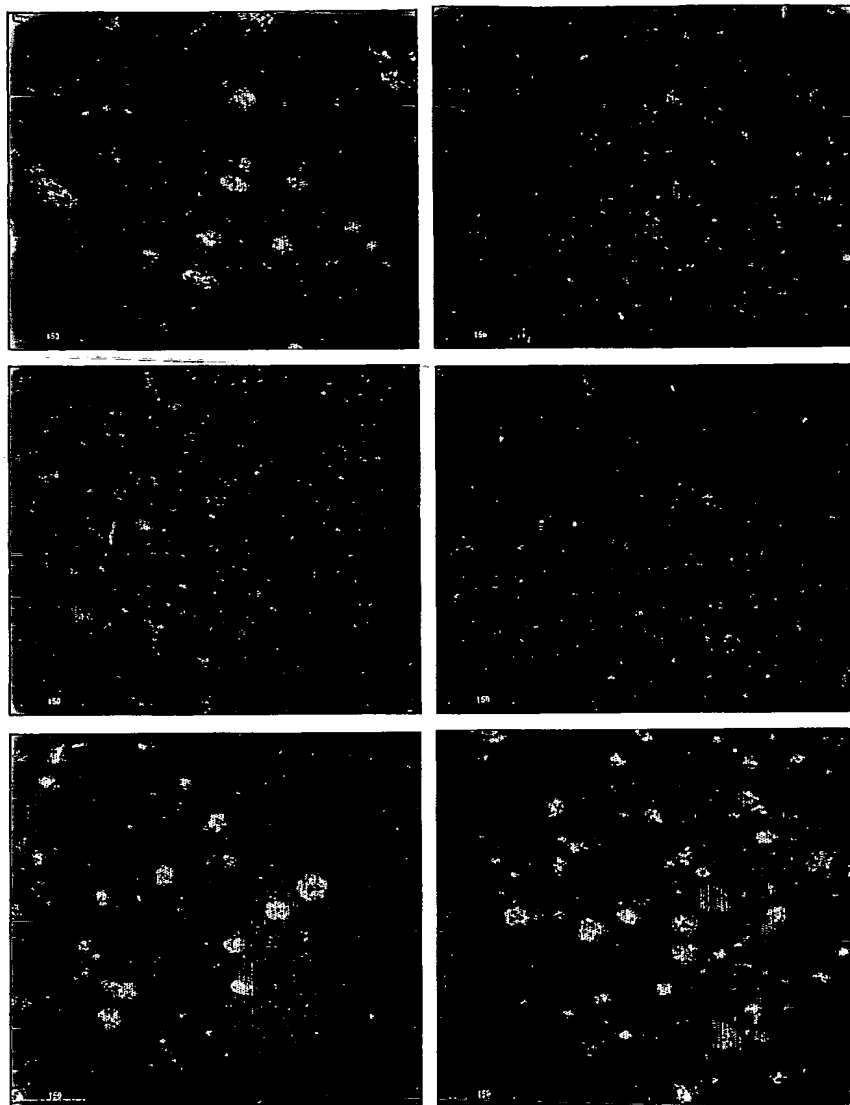
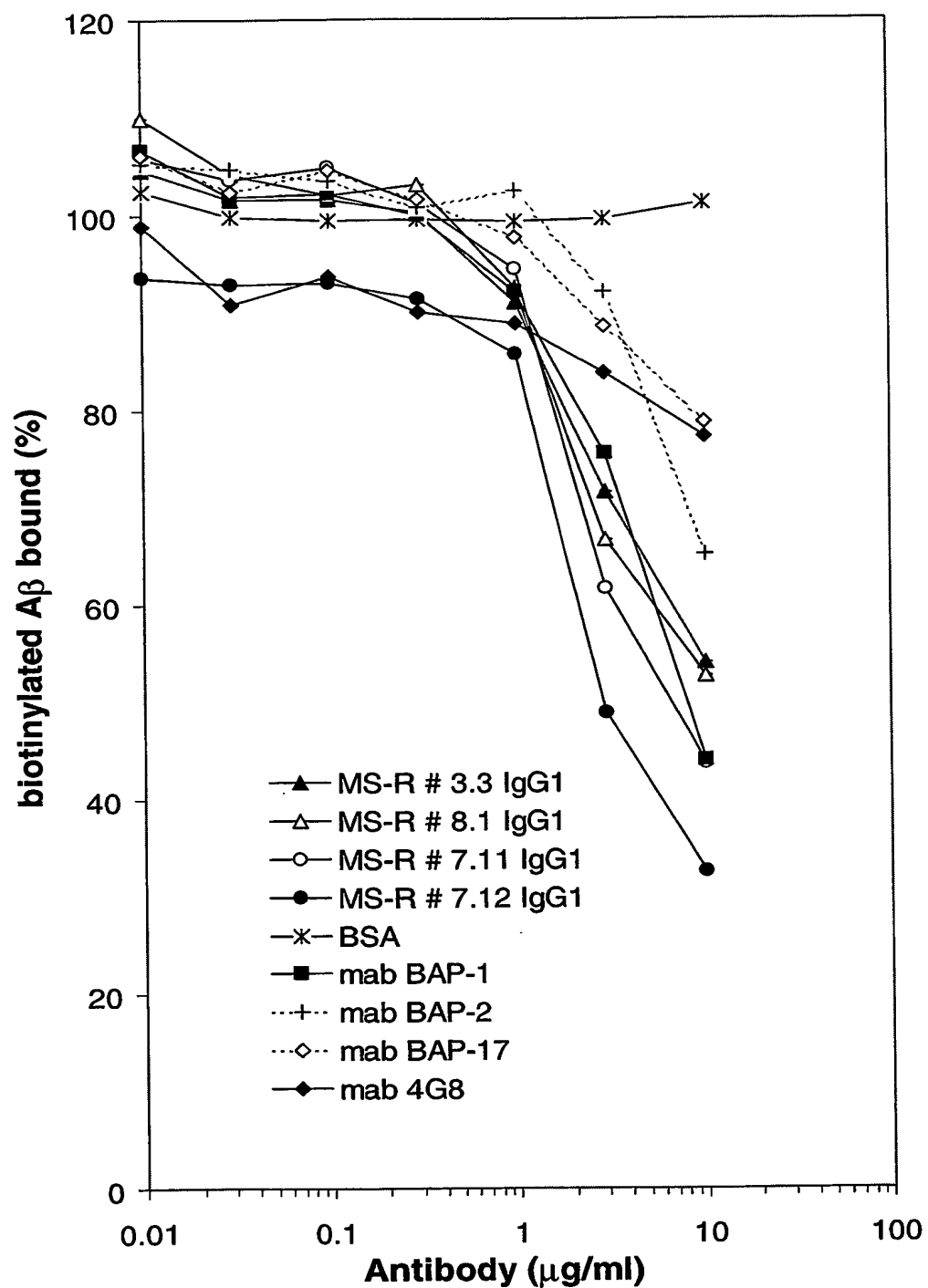
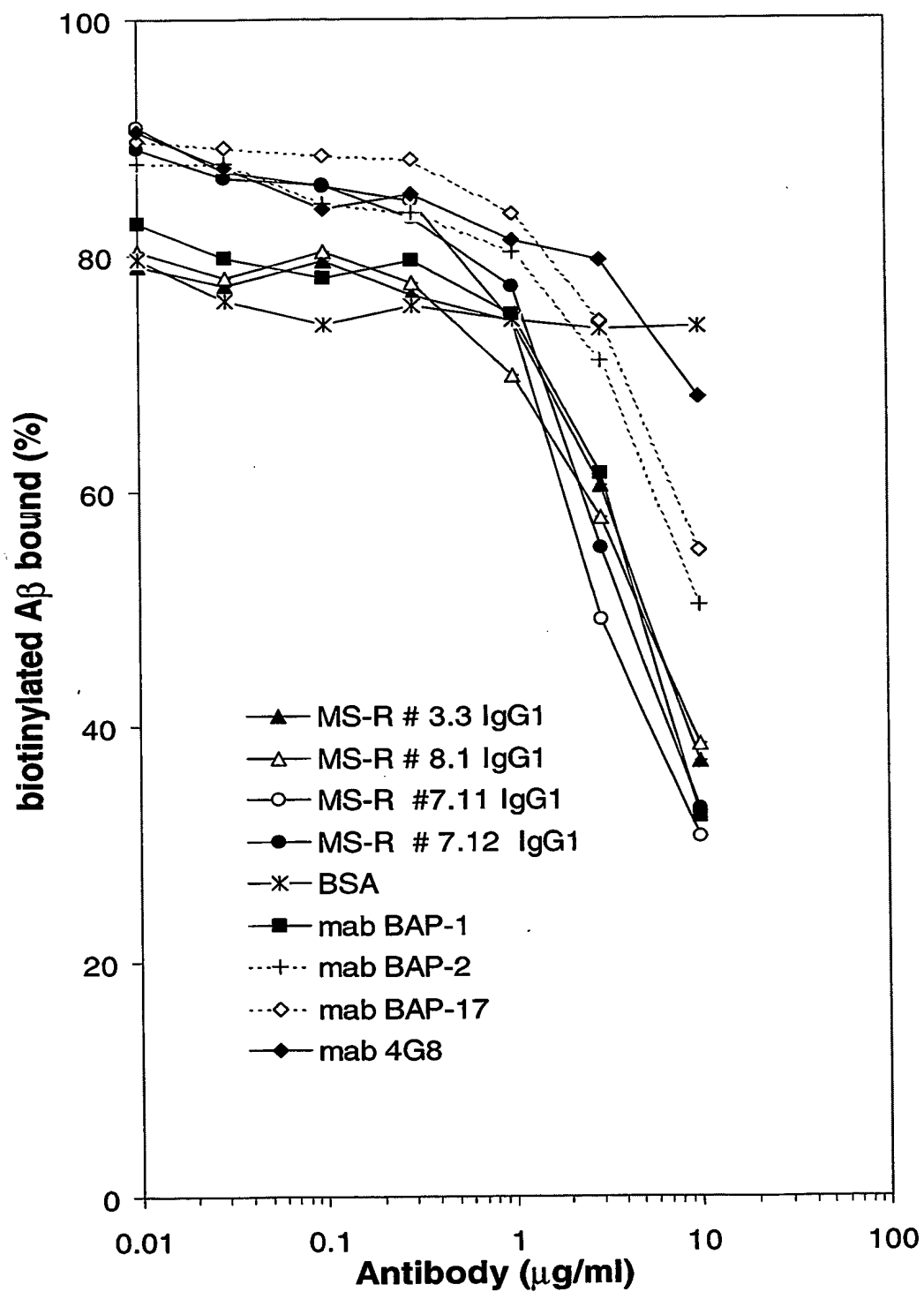


Fig. 8



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Fig. 9A

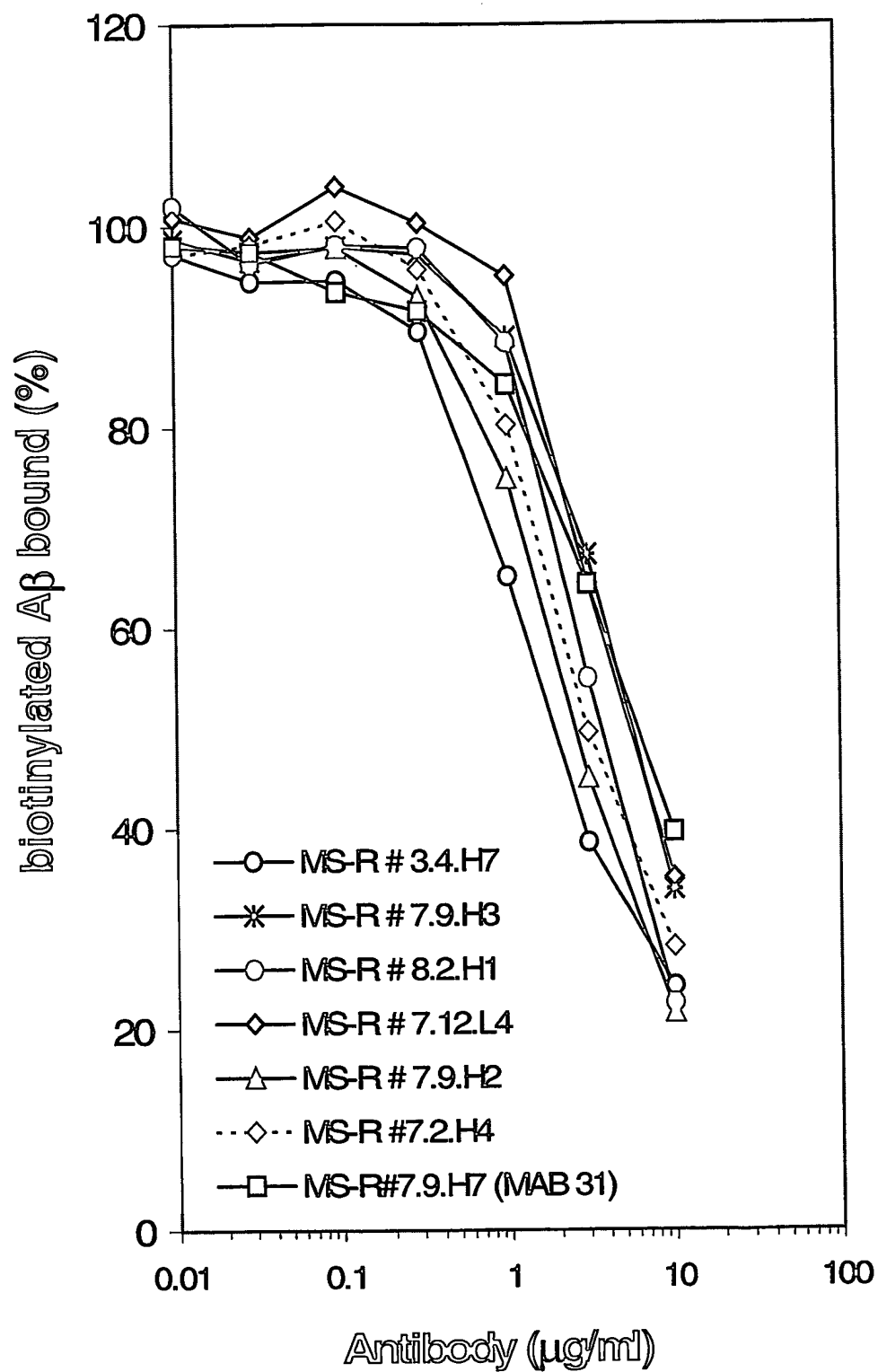
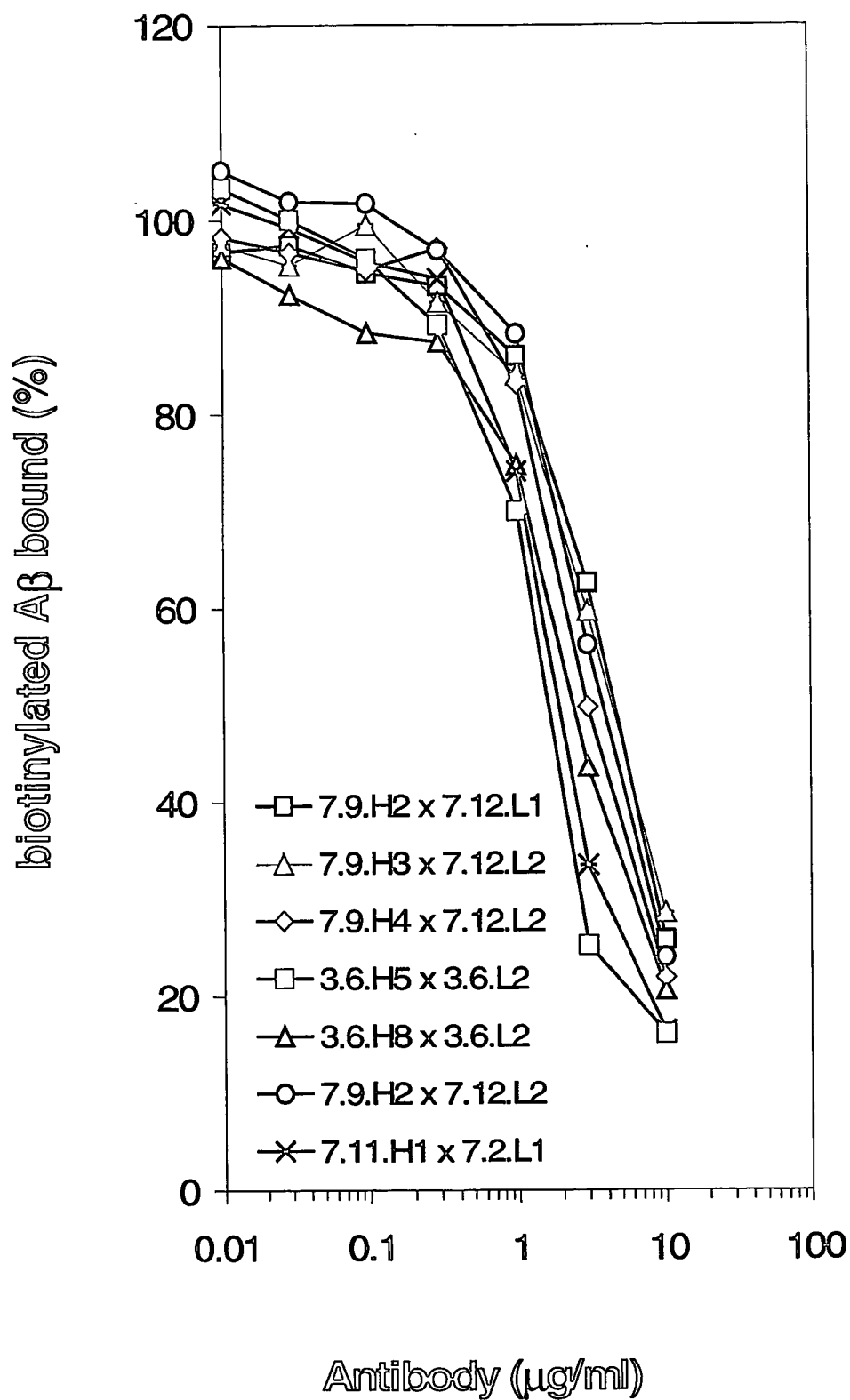
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Fig. 9B

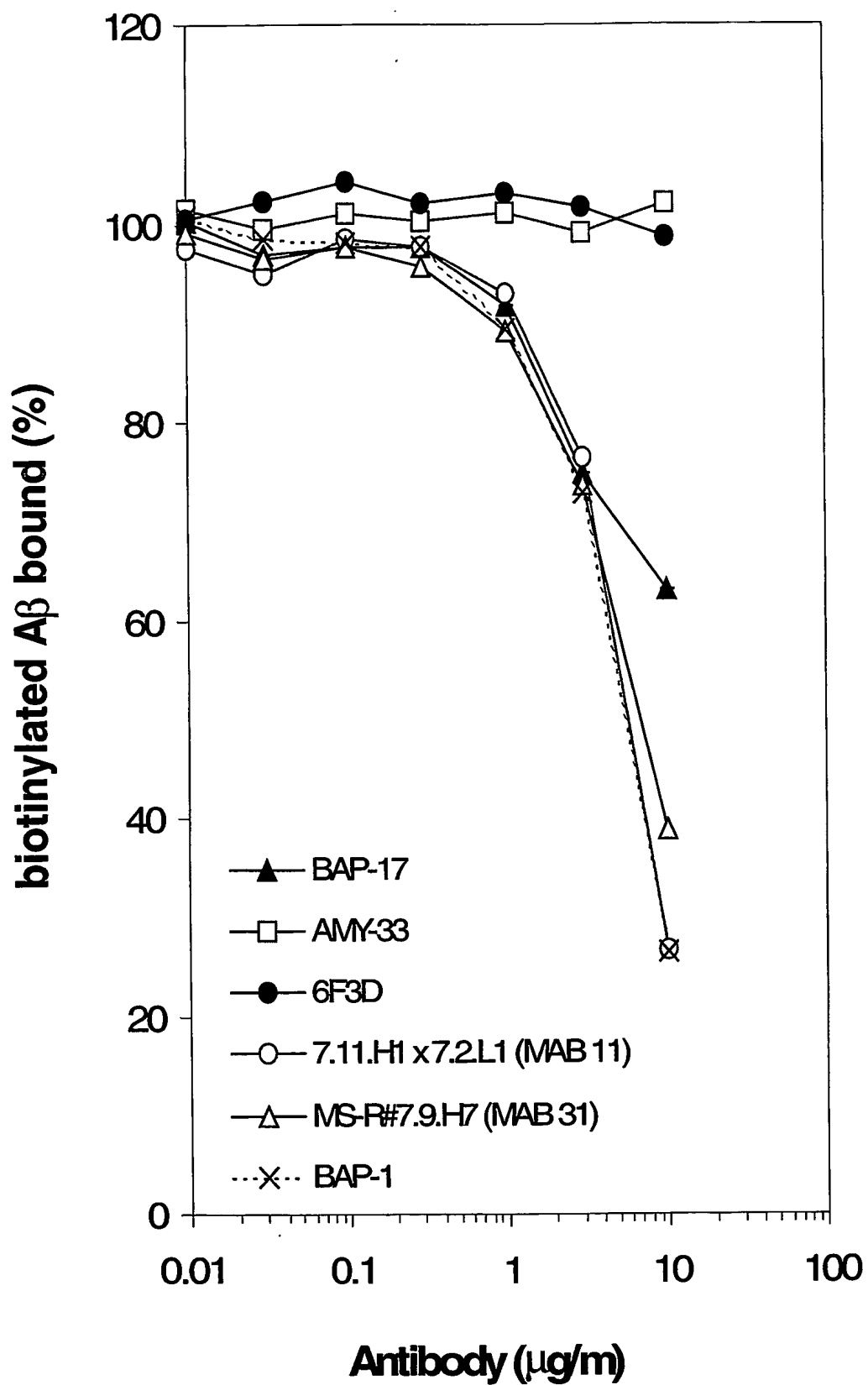


Fig. 9C



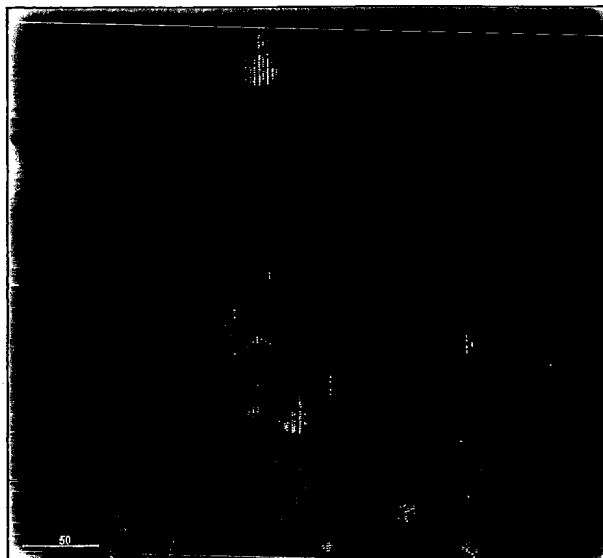
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Fig. 9D



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Fig. 10

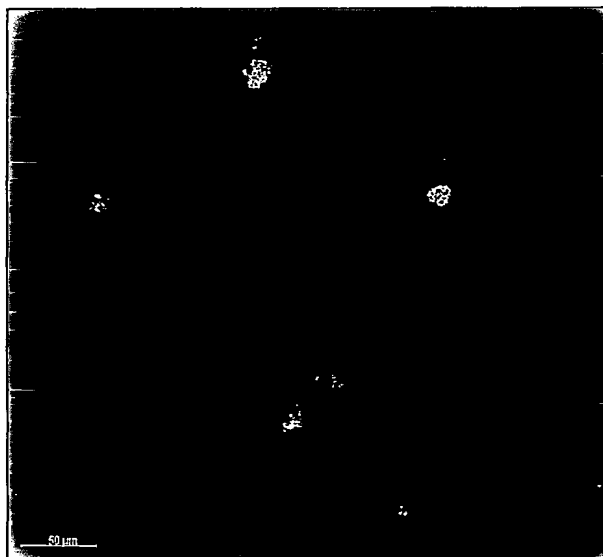
A



B



C

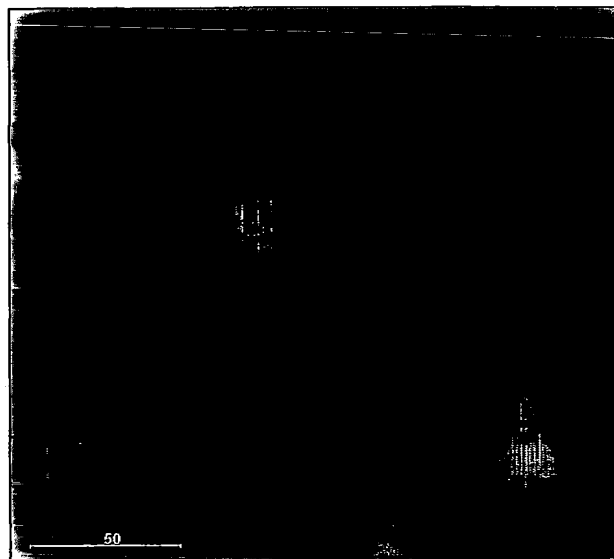


D

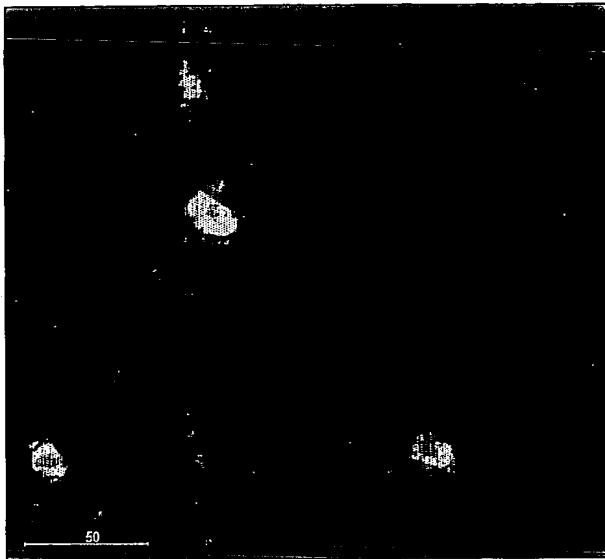


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Fig. 11

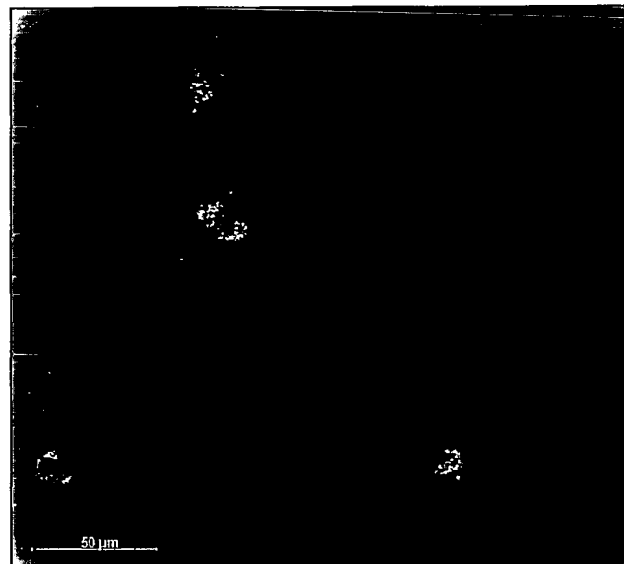
A



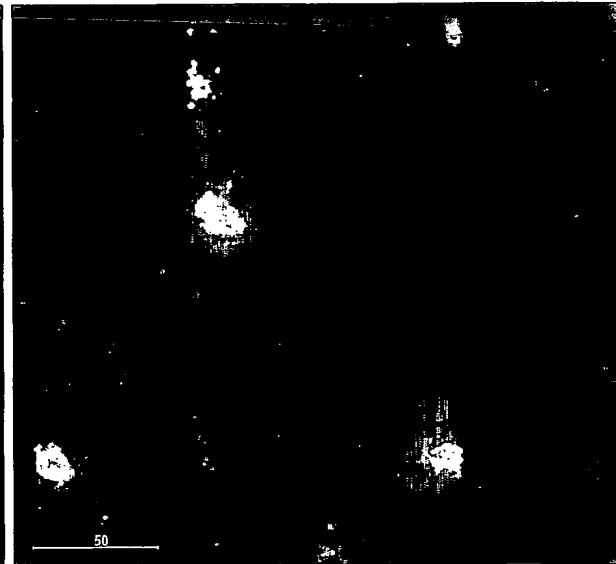
B



C

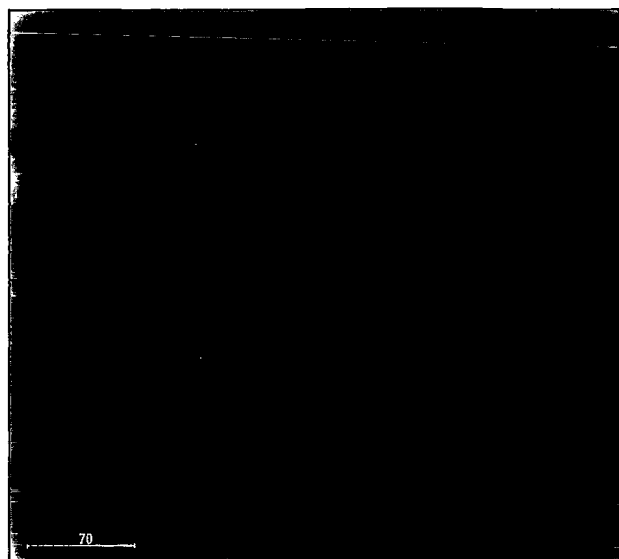


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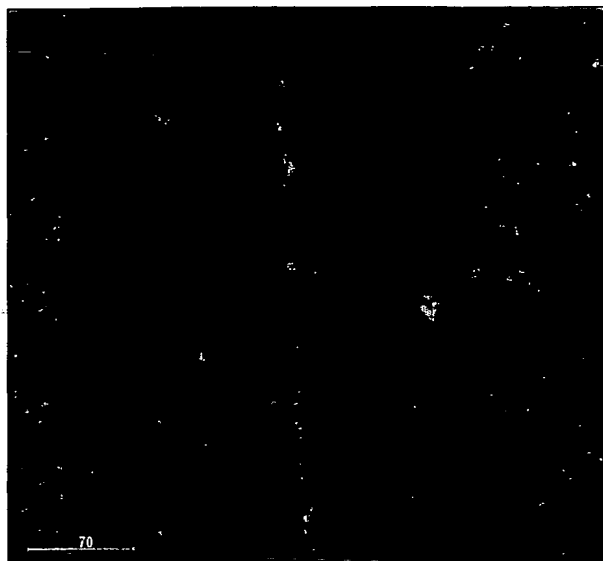


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Fig. 12

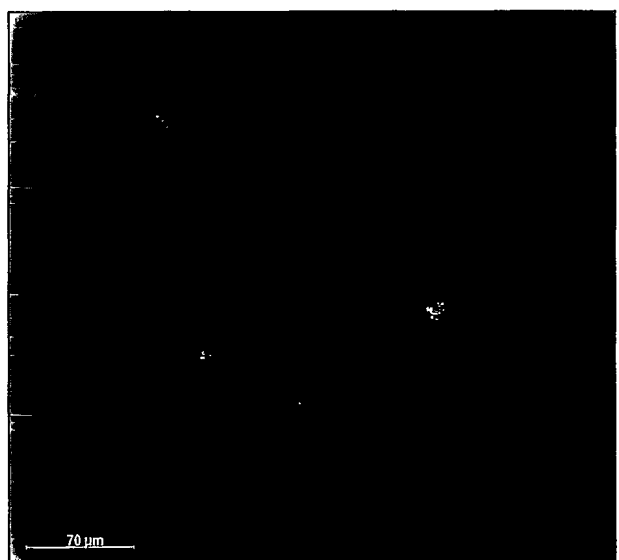
A



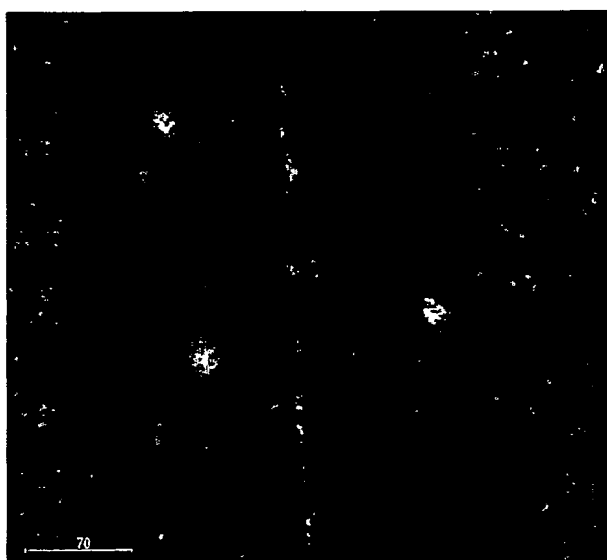
B



C

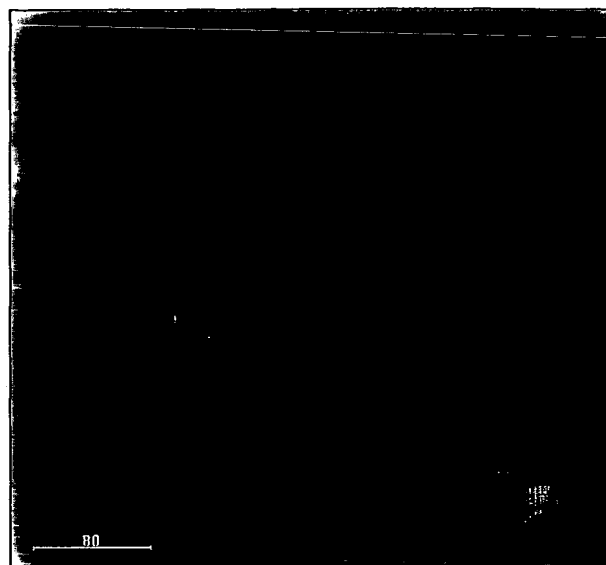


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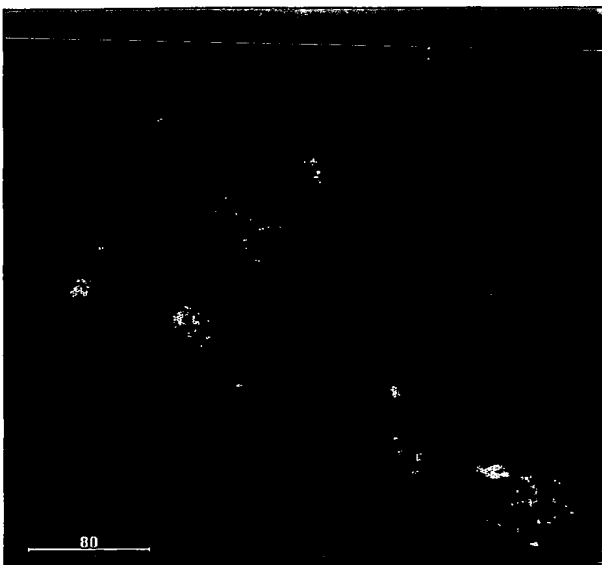


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Fig. 13

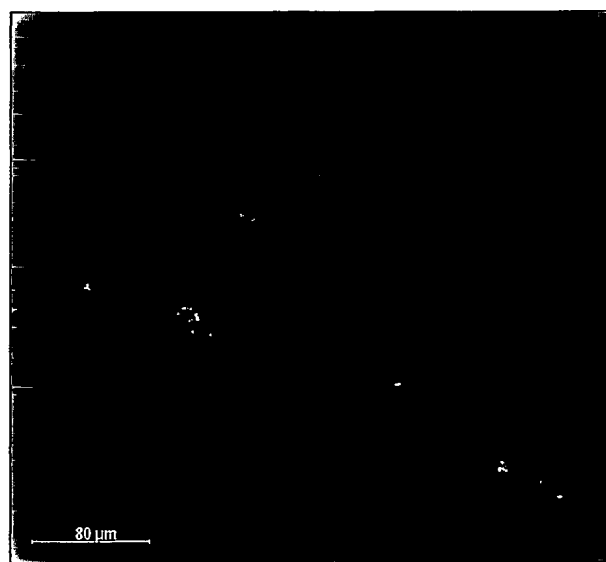
A



B



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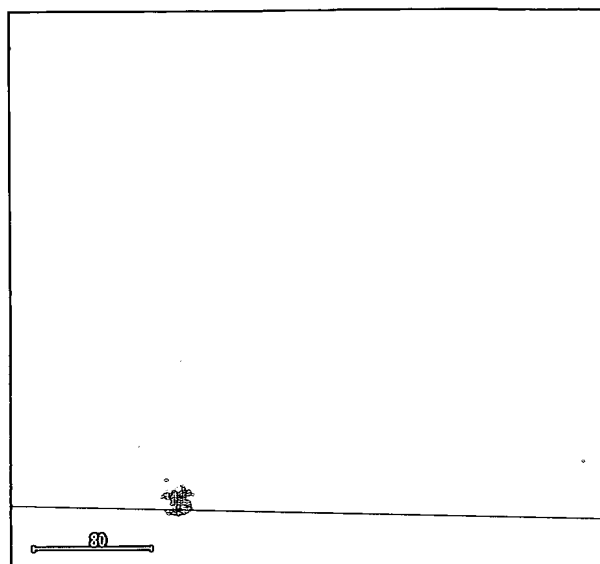


D

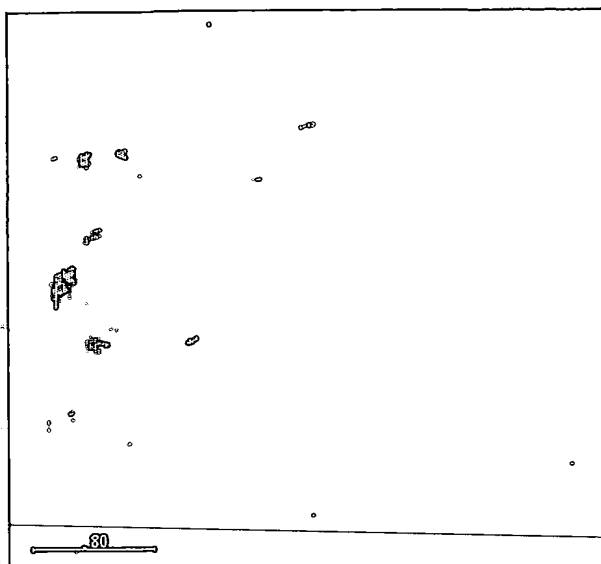


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Fig. 14

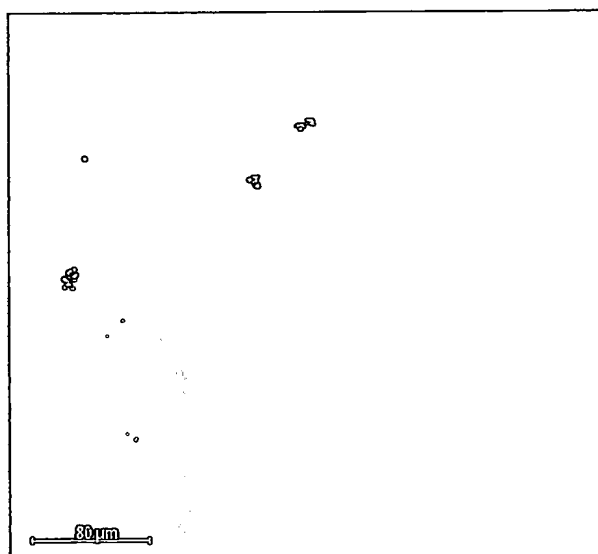
A



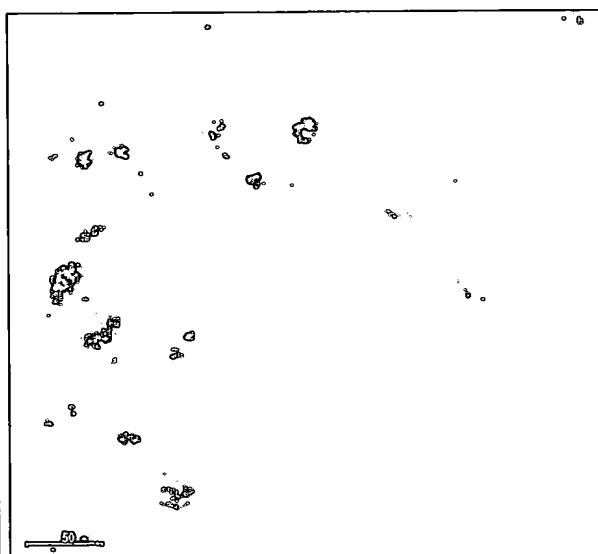
B



C

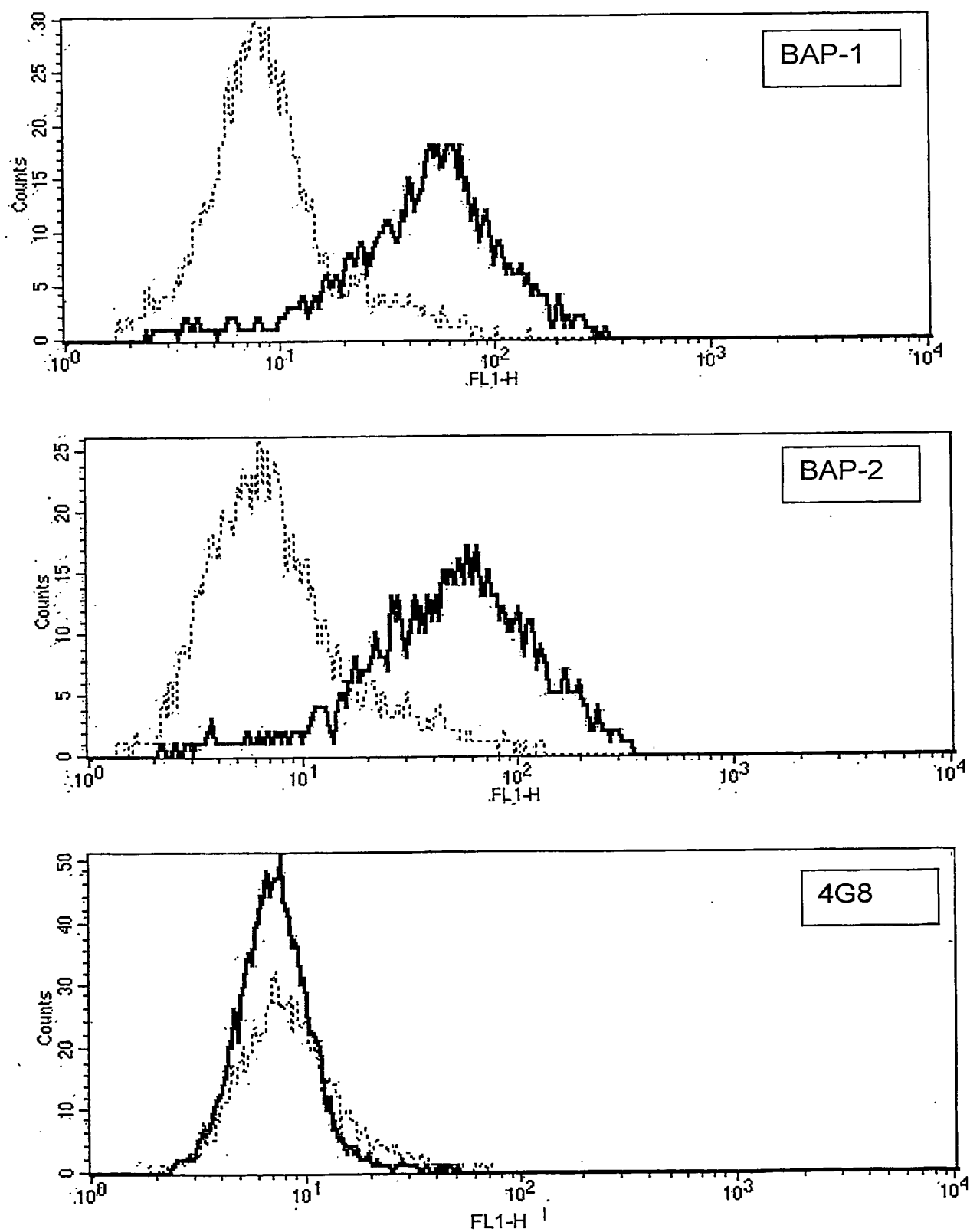


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Fig. 15 - 1





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Fig. 15 - 2

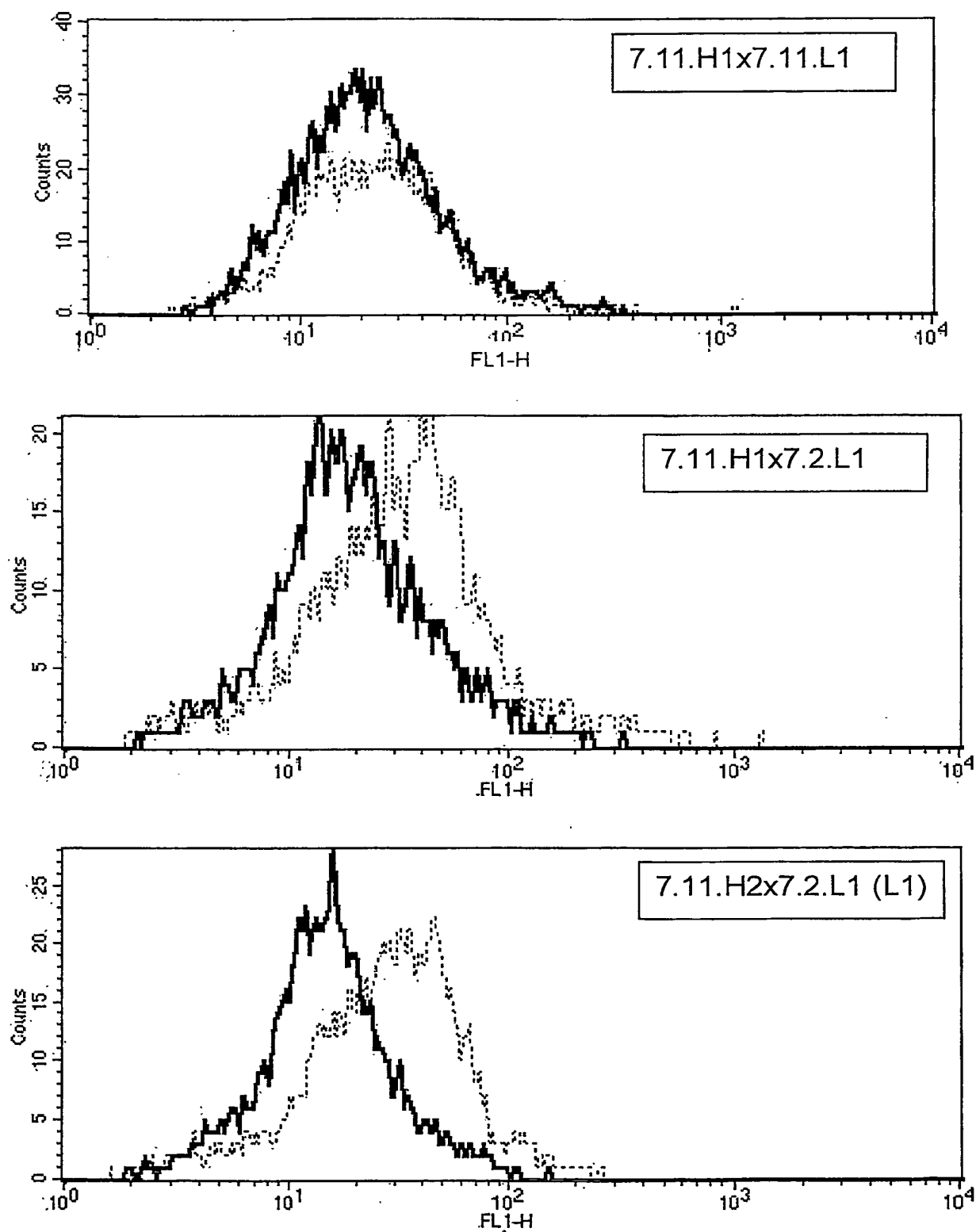


Fig. 15 - 3

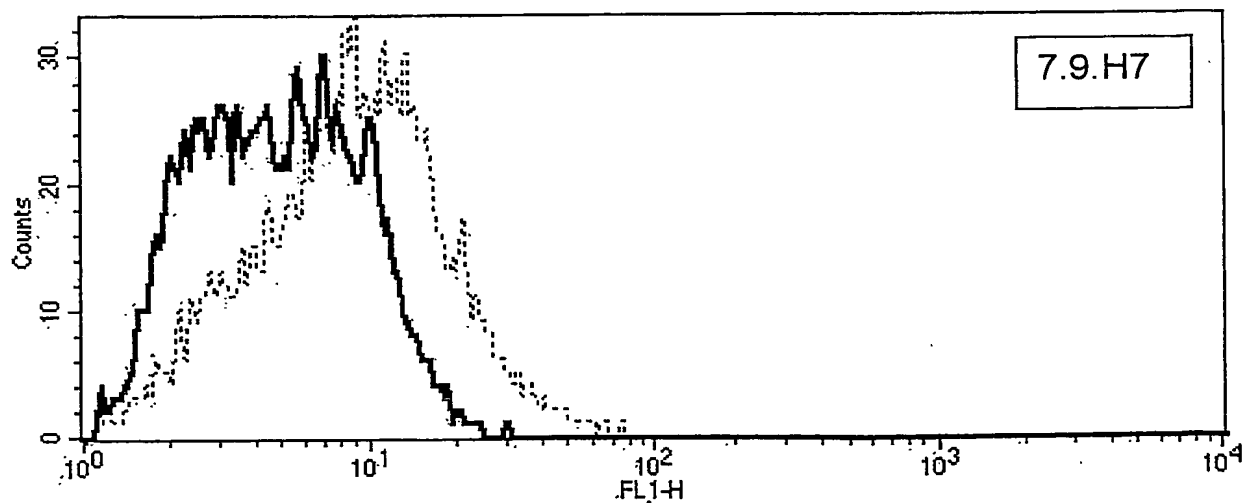
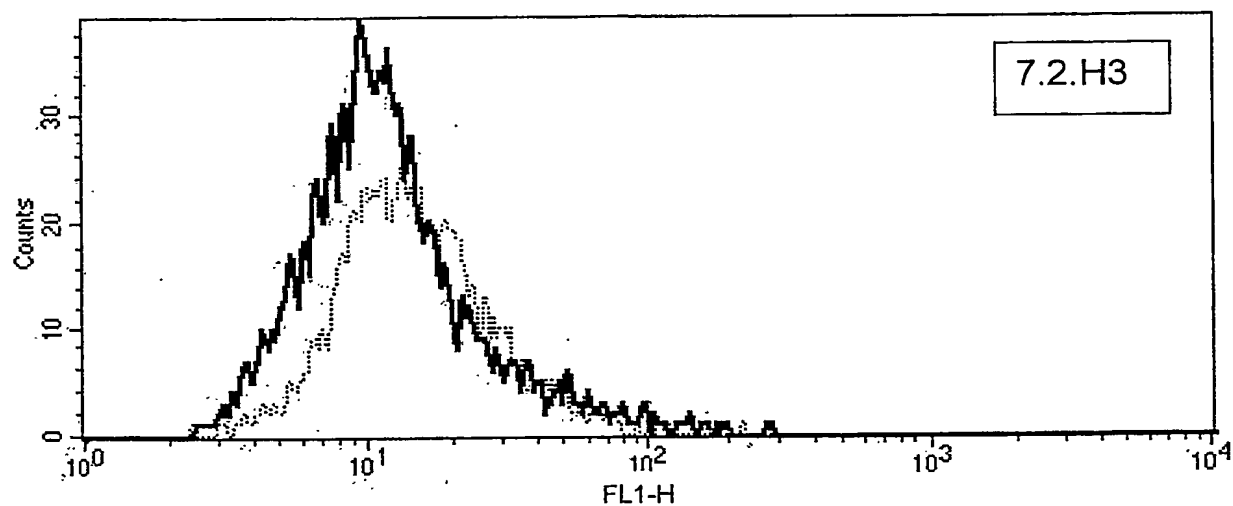
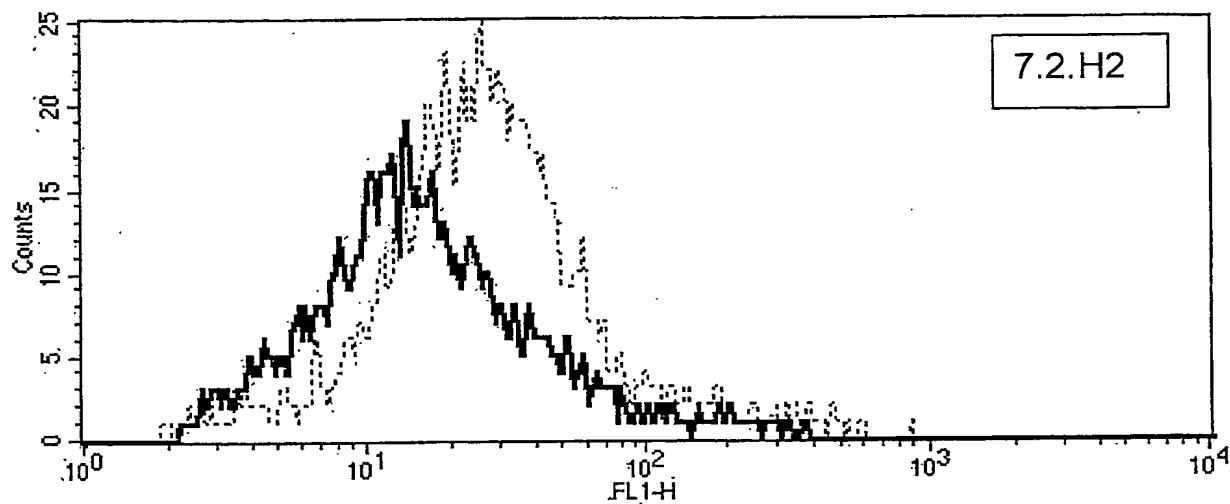
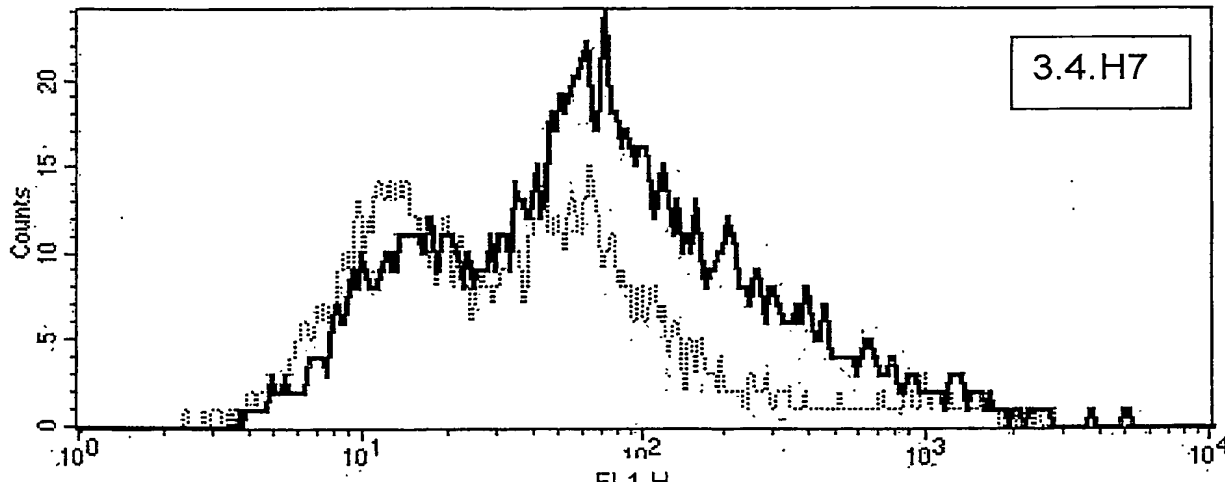
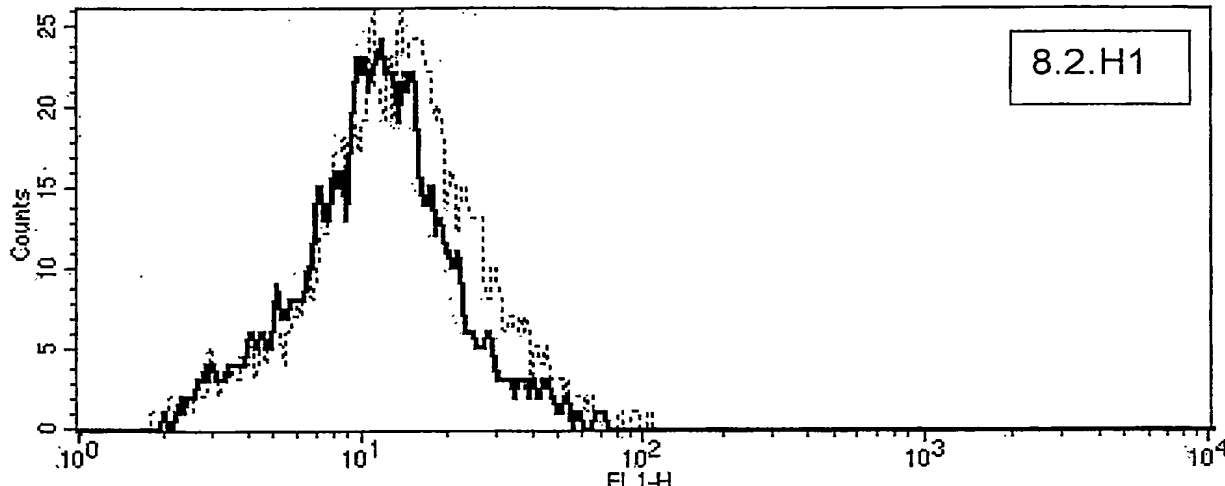


Fig. 15 - 4



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